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Table of Contents

A NEURO-MYO-ARTERIAL GLOMUS IN THE TEMPORO-MANDIBULAR MENISCUS.

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IN previous communications, the writer (Griffin, 1957, 1958) reported diverse symptoms associated with temporo-mandibular joint dysfunction. They seemed to be related to compression of anatomically definable areas of the disc which normally are not compressed during the masticatory reflex. Plastic thrombophlebitis and atherosclerosis (Griffin and Barnett, 1958*a* and *b*) had been reported in these areas, and it was suggested that intermittent compression was a factor in the pathogenesis of these condtions. Griffin (1959*a*) had demonstrated a strategic arterio-venous anastomosis in the capsule of the joint in a fœtus at term, and the neuro-vascular tissue in the vicinity of the attachment of the disc to the squamo-tympanic fissure in the adult has been noted (Griffin and Sharpe, 1960).

The symptoms associated with malposition of the condyle during the masticatory reflex seemed explicable on the basis of stimulation of sympathetic afferent fibres in the above-mentioned areas of the joint reflexly affecting vascular homœostasis (Griffin, 1959*b*), and were cured in certain cases by adjustment of the occlusion; and there was strong evidence that the afferent pathway was via the cephalic extensions of the thoracic spinal nerves (Christenson, 1934; Kuntz, 1934; Kuntz and Main, 1940; Griffin, 1957). This being so, temporo-mandibular joints were removed *post mortem* in an effort to demonstrate a morphological indisputable "trigger mechanism". This "trigger mechanism" was found in the third temporo-mandibular meniscus removed, and turned out to be a small glomus or, more precisely, a neuro-myo-arterial glomus (Masson, 1924). This term implies that it is not actually a neoplasm, and also that it is probably a normal structure in this vicinity.

Histological Findings.

The specimen consisted of a left temporo-mandibular meniscus removed *post mortem* from a male cadaver, aged 58 years. It was orientated as nearly as possible in the sagittal plane, and sections were cut at intervals of 10μ.

A neuro-myo-arterial glomus was located at the postero-medial margin of the disc, in the vicinity of its attachment to the squamo-tympanic fissure. The glomus consists of the afferent artery which has been termed the preglomerular artery, periglomerular arterioles, periglomerular capillaries, periglomerular veins, the Sucquet-Hoyer canal, the receptaculum or collecting vein, and the periglomerular nerve. A schematic reconstruction (Figure I) shows the relationship of these structures

to each other and the relation of the glomus to the synovial vascular system. The lines through the reconstruction indicate selected areas where photomicrographs have been taken.

The preglomerular artery is specialized by the fact that it has a subendothelial coat of longitudinal muscle cells. The disposition of the intimal longitudinal muscle cells results in intimal cushions (Figure XIII[1]), which appear characteristic of this type of artery (Popoff, 1935). The preglomerular artery gives rise to periglomerular arterioles and the artery destined to supply the synovial membrane in this area. These vessels do not appear to have any specialized type of structure. The terminal periglomerular arterioles enter the capsule of the Sucquet-Hoyer canal, some becoming continuous with it, whilst others, though entering the capsule of the canal, do not empty into it but anastomose with periglomerular veins which run parallel to the canal and subsequently empty into the receptaculum (Figures IV, V, VI, VII, VIII). Periglomerular arterioles also give rise to a capillary system associated with the wall of the receptaculum and the periglomerular nerve (Figure XII), which eventually terminate in periglomerular veins.

The Sucquet-Hoyer canal (Figures II, III, IV, V, VI, VII) is characterized by the presence of epithelioid cells in its wall, by its corrugated lumen and by the absence of an internal elastic lamina. The epithelioid cells have central nuclei and poorly-staining cytoplasm, which give in an appropriate section a halo effect (Figure VI). Modified muscle cells are apparent in the arterial segment of the canal, the epithelioid cells being more numerous in its venous segment. Its external coat consists of a neuro-collagenous reticulum (Popoff, 1935).

The receptaculum is a fairly thin-walled vein, but the thickness of its wall is increased in places by associated periglomerular blood vessels (Figures VIII, X). It is continuous with the Sucquet-Hoyer canal, and receives veins from the synovial membrane and periglomerular veins (Figure IX). It is innervated by the periglomerular nerve, so that in a sense its external coat consists of a neuro-collagenous reticulum.

The periglomerular nerve is intimately associated with the glomus, and in cross section it is seen to exhibit some large myelinated nerve fibres, the remainder being amyelinate.

The intimate relationship of nerves to arterio-venous anastomoses of the epithelioid type has been described in man (Masson, 1935, 1936, 1937; Popoff, 1935; Hett, 1934; Schorn, 1955), in the dog's tongue (Brown, 1937), in the sheep (Prichard and Daniel, 1954) and in the glomus caroticum of cats (De Castro, 1951). Periglomerular capillaries are intimately associated with the periglomerular nerve.

Discussion.

The features of the vascular system are the cushioned afferent artery, the epithelioid cell type of the Sucquet-Hoyer canal, the receptaculum which receives its venous return from the synovial membrane, the afferent artery, and the Sucquet-Hoyer canal and the intimately associated periglomerular nerve.

Concerning intimal cushions of afferent arteries in glomus bodies in the finger-tips, Popoff (1935) writes: "*Les soulèvements endothéliomusculaires jouent apparemment le rôle de valvules, dirigeant le sang dans les canaux de Sucquet-Hoyer ou dans les artères préglomérulaires.*" There seems no doubt that the structure of the afferent artery is to regulate the flow of blood both to the synovial membrane and through the by-pass vascular canals. The Sucquet-Hoyer canal at its venous end exhibits numerous epithelioid cells. According to von Schumacher (1938), these cells have both a local mechanical action and a secretory function. The origin of epithelioid cells assumes some importance when the origin of glomus tumours is considered. For von Schumacher (1907, 1915), Krompecher (1932), Mathis (1934), Clara (1939) and Gasparini and Bucciante (1950), epithelioid cells and smooth muscle cells originate from the same type of mesenchymal cell. Von Rotter (1950) and von Rotter and Wagner (1952) are of the opinion that epithelioid cells differentiate from a mesenchymal syncytium and are recognizable in 27 to 30 cm. fœtuses. King (1954) stated: "It is important to realize that the development of any of these cells is dependent on the particular stimuli which are acting on the tissues and is not an inherent function of the cells themselves." According to the writer's observation (unpublished), epithelioid cells are very common in the human temporo-mandibular meniscus at the age of two years, but are rare at term. Muratori (1945, 1946) has observed cushioned arteries terminating in veins in the human pulvinar acetabulum and synovial membrane, and has noted epithelioid cells at the terminal portion of the cushioned artery. Thus a similar vascular architecture would appear to exist in the pulvinar acetabulum as in the temporo-mandibular meniscus. Lang (1954), by an injection method, has demonstrated arterio-venous anastomoses in the interphalangeal joints of the great toe. Luna (1951) similarly demonstrated arterio-venous anastomoses

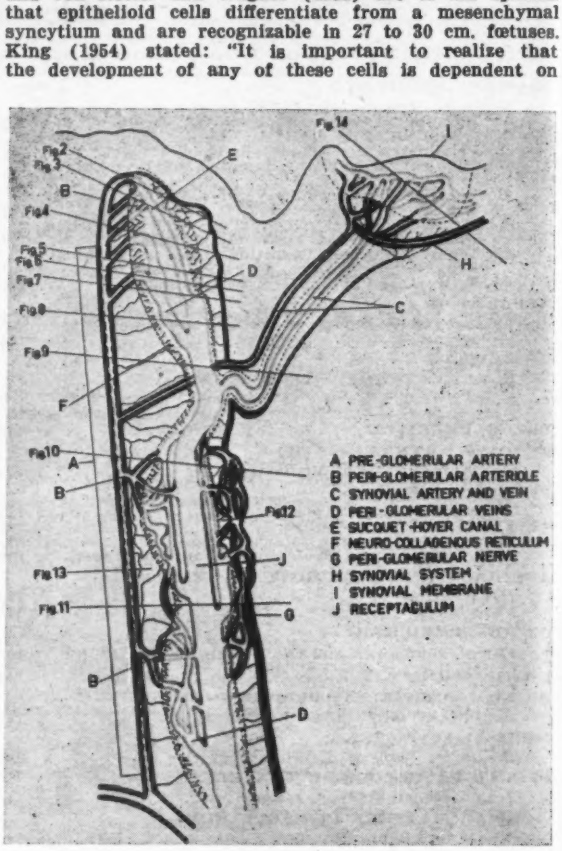

FIGURE I.

A schematic reconstruction of a neuro-myo-arterial glomus from the region of the human temporo-mandibular meniscus in the vicinity of its postero-medial attachment to the squamo-tympanic fissure. The preglomerular artery (A) divides into periglomerular arterioles (B), and an artery (C) which supplies the synovial membrane (I). The periglomerular arterioles anastomose with the Sucquet-Hoyer canal (E) and the receptaculum (J), and also give rise to a capillary system which empties by periglomerular veins or venules (D) into the receptaculum, and which is intimately associated with the periglomerular nerve (G). The periglomerular nerve innervates the Sucquet-Hoyer canal, the wall of the receptaculum and the synovial system. The lines through the reconstruction indicate approximate planes of selected areas where photomicrographs have been taken. For the purpose of clarity some of the vessels are out of proportion.

[1] For Figures II to XIV see art-paper supplement.

in the human knee joint. It seems probable, therefore, that glomus tumours described in knee joints (Butz, 1940; Hoffman and Ghormley, 1941; Mackey and Lindrum, 1936; Lewis and Geschickter, 1935), in the wrist joint (Lewis and Geschickter, 1935; Butz, 1940) and in the bones of the foot (Bergstrand, 1937) arise from proliferation of preexisting epithelioid cells.

The rich innervation of the blood-vessels constituting the glomus can be inferred by the intimate relationship of the periglomerular nerve which consists of myelinate and amyelinate nerve fibres. Clara (1956) quotes Masson (1924) as follows: ". . . *que les distensions vasculaires perçues par les fibres sensorielles extravasculaires puissent être l'origine d'un réflexe moteur et que les contractions extrêmes perçues par les terminaisons intrapariétales puissent être l'origine d'un réflexe inhibiteur: ainsi se compendraient les alternances rythmiques systoles et diastoles glomique. On peut penser aussi que les pressions perçues par les corpuscles tactiles dermiques puissent, elles aussi, être l'origin de réflexes contractiles inhibiteur glomo-glomique.*" Popoff (1935) writes: "*La structure neuromusculaire explique les particularités de sa contraction observies in vivo (Clark). Le système glomérulaire intervient dans deux functions, l'une locale et l'autre générale.*"

It would seem, therefore, that the local function of glomus bodies in joints is to regulate the blood flow to the synovial membrane, at the same time to maintain a fairly constant peripheral resistance and thus to play a role in the maintenance of blood pressure. It is also probable that they control the temperature of joints located near the surface, since they have the ability greatly to increase the blood flow through the part.

It is also probable that the afferent nerve fibres found in glomus bodies participate in neuro-vascular reflexes (Brown, 1937), and certain of the symptoms associated with glomus tumours are undoubtedly reflex in nature (King, 1955). In this respect it seems likely that certain of the symptoms associated wth temporo-mandibular joint dysfunction are explicable on the basis of intermittent compression of neuro-vascular tissue in certain areas of the meniscus which are not usually under compression. The most common symptoms are ipsilateral acroparæsthesia, muscular rigidity, limitation of movement of the shoulder joint and pain in the upper extremities, head, neck and thorax. Associated symptoms are tinnitus and vertigo (Griffin, 1957, 1958). The diagnosis is based on depression of the mandibular condyle and partial immobilization of the mandible by inserting bite blocks, with disappearance of symptoms.

Summary.

1. A neuro-myo-arterial glomus has been described in the vicinity of the attachment of the temporo-mandibular meniscus to the squamo-tympanic fissure.

2. The function of the glomus has been discussed.

3. It is suggested that certain symptoms associated with temporo-mandibular joint dysfunction are due to compression of the neuro-vascular tissue in certain areas of the disc.

Acknowledgement.

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Legends to Illustrations.

FIGURE II(A).—The arteriole (B) is in the wall of the Sucquet-Hoyer canal (E). The Sucquet-Hoyer canal (E) has no internal elastic membranes. (Hæmatoxylin and van Gieson stain, × 120.)

FIGURE (IIB).—A periglomerular arteriole (B) is entering the wall of the Sucquet-Hoyer canal (E). Smooth muscle cells (M)

can be seen in the wall of the blood vessel. (Hæmatoxylin and van Gieson stain, × 120.)

FIGURE III.—An arteriole (B) in the wall of the Sucquet-Hoyer canal (E). (Hæmatoxylin and van Gieson stain, × 120.)

FIGURE IV.—The arteriole has anastomosed with a vein (D). Note the corrugated appearance of the lumen of the Sucquet-Hoyer canal (E). (Hæmatoxylin and van Gieson stain, × 120.)

FIGURE V.—A branch (B) of the preglomerular artery (A) is entering the capsule of the Sucquet-Hoyer canal and anastomosing with the periglomerular vein (D). The lumen of the Sucquet-Hoyer canal (E) is not so corrugated, although there are numerous epithelioid cells in its wall. The periglomerular nerve (G) is in relation to the Sucquet-Hoyer canal. (Hæmatoxylin and phloxin stain × 120.)

FIGURE VI.—The venous part of the Sucquet-Hoyer canal. The epithelioid cells (N) are more numerous and the lumen (E) is more patent. The lumen of the periglomerular vein (D) has increased in diameter and the periglomerular nerve (G) is seen in transverse section. (Hæmatoxylin and phloxin stain, × 120.)

FIGURE VII.—The venous end of the Sucquet-Hoyer canal (E) cut into obliquely longitudinal sections. What are probably myelinated nerve fibres (K) can be seen in its wall, and the relations of the cushioned artery (A) and periglomerular nerve (G) are apparent. (Verhoeff's and van Gieson stain, × 120.)

FIGURE VIII.—The periglomerular vein (O) can be seen entering the receptaculum (J). The constant relationship of the periglomerular artery (A) and nerve (G) is apparent. (Verhoeff's and van Gieson stain, × 120.)

FIGURE IX.—The extension of the receptaculum (C), which receives veins from the synovial membrane and the artery (C) supplying the synovial membrane, can be seen. The receptaculum proper (J) is inferior to its synovial extension. (Hæmatoxylin and van Gieson stain, × 120.)

FIGURE X.—This section demonstrates the intimate relationship of the periglomerular nerve (G) to the receptaculum (J), the associated periglomerular veins (D) and the preglomerular artery (A). (Verhoeff's and van Gieson stain, × 120.)

FIGURE XI.—This section shows a small vein entering the receptaculum. (Hæmatoxylin and van Gieson stain, × 120.)

FIGURE XII.—This section shows the relationship of the periglomerular nerve (G) to associated blood vessels and the receptaculum (J). (Hæmatoxylin and van Gieson stain, × 400.)

FIGURE XIII.—Transverse section through the preglomerular artery (A) and a periglomerular arteriole (B). The subendothelial longitudinal smooth-muscle fibres (L) can be seen on the lumen side of the internal elastic membrane. (Hæmatoxylin and van Gieson stain, × 400.)

FIGURE XIV.—The synovial vascular system. (Verhoeff's and van Gieson stain, × 400.)

RADIATION HAZARDS TO THE FŒTUS FROM X-RAY PELVIMETRY.

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THE information provided by X-ray pelvimetry materially aids in the successful conduct of a pregnancy when the examination is carried out for cogent obstetrical reasons. However, Stewart *et alii* (1956) seriously questioned the safety of X-ray pelvimetry by reporting a twofold increase in childhood leukæmia when the developing fœtus had been exposed to diagnostic irradiation. Dorothy D. Ford (1959) presented a series of 78 children aged under 10 years suffering from leukæmia, 21 of whom had been exposed to irradiation in the third trimester of their intrauterine existence. The Medical Research Council (1956), in "The Hazards to Man of Nuclear and Allied Radiation", reached a similar general conclusion—that leukæmia was more frequent in Hiroshima and Nagasaki as a result of irradiation received by the survivors of the 1945 atomic bomb explosions.

This concept of the deleterious effects of irradiation on the developing fœtus was formulated earlier by Murphy (1930), who indicated that therapeutic irradiation of the maternal pelvis increased the incidence of abortion, premature labour and fœtal anomalies. Yet none of the available information applies specifically to the problem facing the obstetrician who wishes to balance the value of the information obtained by an X-ray pelvimetry with the conjectured deleterious effects on the unborn child.

In an attempt to provide some practical information on this subject, a retrospective survey was carried out on the offspring of the 643 mothers who were subjected to an X-ray pelvimetry at the Royal Women's Hospital, Melbourne, between 1945 and 1955. In these cases, the examination was carried out in the third trimester, and the average doses of irradiation received by the left and right ovary were 10*r* and 2·6*r* respectively. This dosage cannot be readily translated into terms of total fœtal irradiation (Swindon, 1960).

A letter was sent to the last known address of these mothers. Fifty-six unmarried women were excluded from the follow-up investigation, as were those of 18 cases in which a stillbirth or neonatal death occurred. The children of 211 mothers were interviewed, and subjected to a full clinical examination, including urine examination and hæmoglobin estimation. Thirty-four parents indicated that their offspring were healthy, but were unable to bring them for an examination, although most consulted their local medical practitioner before replying to the letter; 180 letters were returned undelivered. A further group of 138 patients presumably received the letter, but neglected to reply.

Results.

The following tabulation shows the response to the initial letter of inquiry.

Personally examined (213 children) ..	211 mothers
Replied stating child alive and well (most examined by own practitioner)	34 mothers
Letters unanswered and not returned	138 mothers
Letters returned undelivered	180 mothers
Stillbirths	15 mothers
Neonatal deaths	3 mothers
Subsequent deaths	6 mothers
Unmarried mothers (no letter sent) ..	56 mothers
Total pelvimetries:	643

Table I gives the causes of the 24 stillbirths, neonatal deaths and subsequent childhood deaths in the series. The six abnormalities found in 245 survivors are also listed.

Only one case of leukæmia was located. A careful search of the records of the Royal Children's Hospital, Melbourne, and the Royal Women's Hospital, Melbourne, and inquiry from the Victorian Government Statistician (Townsend, 1958) did not disclose that any other patient had died of leukæmia who had been irradiated in utero at the Royal Women's Hospital. A child who had died from leukæmia outside the State of Victoria, or with an erroneous diagnosis in the death certificate, could escape detection in this survey. No other malignant disease was found. Four pregnancies resulted in a congenital anomaly producing stillbirth or subsequent early death, whilst six other patients had anomalies in which X-ray exposure could be ætiologically implicated only as a remote possibility.

Discussion.

A survey of this type can supply limited valid information. The difficulty of matching each irradiated fœtus with a non-irradiated control of similar genetic and environmental background is obvious, and therefore no conclusions on the incidence of congenital anomalies following irradiation can be drawn.

As the oldest patient examined was aged 15 years, it is not surprising that 180 mothers were not located. Among the group of 138 persons who possibly received the letter but failed to acknowledge the fact, it would appear unlikely that there was a disproportionately high incidence of death or sickness, for any inquiry directed towards the possible cause of malignant disease or

TABLE I.

Congenital Abnormalities and Causes of Death following Intrauterine Diagnostic Irradiation.

Stillbirths and Neonatal Deaths.		Childhood Deaths		Abnormalities in Survivors (245 Cases).	
Cause of Death.	Number of Cases.	Cause of Death.	Number of Cases.	Diagnosis.	Number of Cases.
Intrauterine asphyxia	10	Leukæmia	1	Leukæmia and malignant disease	0
Cerebral hæmorrhage	5	Malignant disease	0	Ventricular septal defect	1
Hydrocephalus	1	Microcephaly and cerebral palsy	1	Mental retardation without microcephaly	2
Cleft palate and prematurity	1	Accident	2	Hypospadias	2
Atelectasis	1	Gastro-enteritis	1	Arrested hydrocephalus	1
		Hydrocephalus and myelomeningocele	1		
Total	18		6		6

leukæmia usually receives full support from the relatives in fatal cases.

The practical conclusion does emerge that leukæmia in childhood rarely follows X-ray pelvimetry in the third trimester of pregnancy. As was explained earlier, it is most unlikely that cases of leukæmia have been overlooked.

The absence of other forms of malignant disease cannot be affirmed with such certainty.

In Townsend's series (1958), X-ray exposure as a cause of leukæmia in childhood could be entirely excluded in 93% of cases. In Stewart's series, 85% of children with leukæmia were at no time exposed to intrauterine irradiation, and of the patients of Dorothy Ford, 72% were in a similar category.

It must be stressed that the increased incidence of leukæmia in Hiroshima and Nagasaki in 1945 followed intense irradiation of the survivors, and the deleterious effects observed by Murphy (1930) applied specifically to therapeutic irradiation of the mother's pelvis. These large doses have little relationship to the comparatively small dose administered for diagnostic purposes. Furthermore, the increased incidence of leukæmia was reported by Stewart from a relatively small series of cases, the statistical value of which may be seriously questioned.

Exposure of the fœtus to ionizing radiation may be deleterious in one of two ways: (*a*) It may produce leukæmia or other malignant change. In the children under discussion here, this effect would be expected within a decade of exposure. (*b*) It may induce unfavourable genetic mutations. The final evaluation of these chromosomal changes in the patient, his progeny and the population in general will require many generations to evaluate fully. This genetic effect is not likely to be of importance in diagnostic radiology, provided exposure is restricted to a minimum in each case, and the percentage of the population who are receiving gonadal irradiation is maintained at a low figure (Osborne and Smith, 1956). The Medical Research Council Report makes the following statements:

> For levels of radiation up to the doubling dose and even some way beyond, the genetic effects are only appreciable when reckoned over the population as a whole and need cause no alarm to the individual on his own account . . . A large proportion of the genetically significant dose derived from diagnostic radiology is contributed by a relatively few types of examination, of which fluoroscopic and radiological examination of the female pelvis and examination of the hip joint and lumbar spine in males are important examples. Clearly, the small genetic risk to the community and to individuals must be weighed against the possible great advantage and even necessity of the radiological examination to the particular patient. The final decision must be made on medical grounds.

Conclusion.

X-ray pelvimetry may be regarded as a relatively safe investigation if carried out in the last trimester of pregnancy, with all possible technical safeguards to reduce direct and scatter irradiation to a minimum. That there is a slight risk of the irradiated fœtus subsequently developing leukæmia, neoplastic disease or congenital anomalies is certainly not denied; but this risk appears to be greatly outweighed by the possible benefits to the mother and baby. It must be stressed that X-ray pelvimetry should not be undertaken without adequate obstetric indications, but there is certainly no reason to deny this investigation to appropriate pregnant patients.

Summary.

1. In a series of 643 infants irradiated during X-ray pelvimetry in the third trimester of pregnancy, one case of leukæmia was found.

2. In the same series, nine patients had congenital anomalies, of which four were fatal.

3. It is concluded that the advantages of X-ray pelvimetry in patients with cephalopelvic disproportion outweigh the possible remote dangers.

Acknowledgements.

This survey follows extensive preliminary work by Dr. C. MacDonald, Mr. T. N. Swindon and Professor S. Lance Townsend, and their initial work and help in preparation of this manuscript are gratefully acknowledged.

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NEUROLOGICAL SEQUELÆ OF JAUNDICE OF PREMATURITY.[1]

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INCREASING evidence has been accumulating over the past 15 years that brain damage may occur in the neonatal period as a result of jaundice not due to hæmolytic disease. The first recorded case was that mentioned

[1] Read at a meeting of the Pædiatric Society of Victoria on May 11, 1960.

by Baar in 1945. A year later Parsons (1946) reported a second case in which isoimmunization to the Rh factor was excluded by serological tests. In 1950 Gerrard, also from Birmingham, reported nine premature infants among 43 cases of kernicterus occurring over the preceding five years. Aidin and co-workers (1950) in the same year, found 25 premature infants with kernicterus in 239 consecutive autopsies, including 144 premature infants. There were only 14 infants who died of kernicterus due to Rh-factor iso-immunization.

Simultaneously, Zuelzer and Mudgett (1950) in America reported 55 autopsy cases of kernicterus occurring over 10 years, in 32 of which no evidence of Rh incompatibility was found. These subjects were mostly premature infants, but sepsis was frequently found. ABO incompatibility was not considered significant, though the incidence of incompatibility was higher than expected.

Thus it became apparent that Rh-factor iso-immunization, instead of being the sole cause of kernicterus (as believed by Parsons in 1946), is less frequently responsible than prematurity.

During the years 1958 and 1959, 25 prematurely born children have been examined at the Cerebral Palsy Clinic at the Royal Children's Hospital or allied clinics, who are affected with neurological disabilities which can be attributed to the harmful effects of jaundice in the neonatal period. Rh-factor iso-immunization has been excluded by serological tests.

Prematurity has been quoted as a frequent ætiological factor in cerebral palsy; its incidence varies in different reports. Asher and Schonnell (1950) indicated that premature birth occurred in 39% of 400 cases of cerebral palsy. Other authorities have found a somewhat lower number.

The graph (Figure 1) and the following tabulation

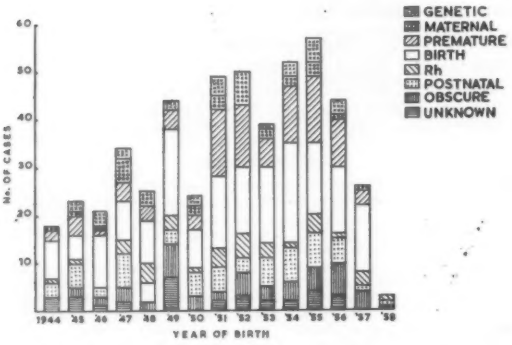

FIGURE I.

show an ætiological analysis of 509 cases of cerebral palsy seen here in 1958, classified according to year of birth and the predominant single ætiological factor.

Genetic factors	29 cases
Maternal factors	31 cases
Prematurity	93 cases
Birth factors	176 cases
Post-natal factors	64 cases
Rh-factor	35 cases
Obscure causes	49 cases
Unknown causes	32 cases
Total:	509

Prematurity was associated in 18·3% of the total number, in 19·7% of the total excluding cases of unknown ætiology, and in 24·0% of the total births since 1950, excluding cases of jaundice of unknown ætiology. Prematurity of 37 weeks' gestation or less is regarded as causative if there is no other apparent cause. Hence the total incidence of prematurity may be somewhat greater than is shown. An increase in the proportion and the total number of affected premature infants is apparent since 1950. The fall off in numbers after 1955 is due to delay in presentation of cases to a special clinic.

Table I is an analysis of 119 premature births defined as above occurring among 606 cerebral palsy patients seen in a two-year period (1958-1959). These are subdivided according to whether athetosis is present and whether a history of jaundice in the neonatal period could be obtained. In many cases it was impossible to obtain reliable information because of lack of records at maternity hospitals, and because the parents were told no details of their baby's progress. The incidence of athetoid cerebral palsy following jaundice in the neonatal period is striking, particularly the rapid rise from 1953 to a peak in 1955. It is hoped the subsequent fall is due to improved understanding and management of jaundice in premature babies, but it may be due to delay in presentation.

The incidence of cerebral palsy due to Rh iso-immunization is included for comparison; and it will be seen incidentally that brain-damaged survivors from this well-understood condition are still appearing.

The clinical features of these two groups are remarkably similar. The predominant type of cerebral palsy seen is athetosis, to which spasticity is added in many of the more severe cases. Ataxia is sometimes present, too. On the whole, in the Rh iso-immunization cases the patients are more severely affected than the premature infants, intellectual defect is more frequent especially as the major disability, and hearing defects are much commoner.

Zuelzer and Mudgett (1950), in their autopsy series, pointed out the similarity in clinical and post-mortem findings in kernicterus of prematurity and kernicterus of Rh iso-immunization. In the latter group there was earlier onset of jaundice, earlier onset of kernicterus and earlier death. The distribution of nuclear staining and nerve-cell damage appeared similar, but cortical damage was rather less frequent in the premature group. Symptoms of kernicterus indicating definite neurological involvement (convulsions, opisthotonos and spasticity) were recorded in only 19 out of their 32 cases. This is in agreement with our findings, in which kernicterus was diagnosed in only 10 cases even when suggestive signs such as drowsiness, poor sucking, irritability and abnormal eye movements were accepted. In four of our cases the records state positively that there were no signs of kernicterus. Jaundice was reported as mild in three cases and moderate in four. Crosse, Meyer and Gerrard (1955), in a study of 60 premature infants with kernicterus, reported that jaundice was not severe in 22.

The findings in the present series are set out in Tables II, III, IV, V and VI. The 25 patients may be divided into two groups — those severely affected physically, of whom there are 11, and the remaining 14 who are mildly affected. Thirteen of the latter had achieved sitting alone by 15 months and walked by three and a half years — the remaining patient will probably achieve these skills within these limits. Of the remainder, one achieved sitting at four years, a few of the others may ultimately sit alone, but none are likely to walk without support. These severly affected children exhibit features of spastic paralysis as well as athetosis, indicating more widespread brain damage.

The intellectual ability of 15 appears normal and a further three are probably of normal or near-normal mentality, but assessment by the Department of Psychiatry is not yet complete. The remaining seven have some degree of mental defect, but this is apparently not gross.

Four children have hearing defects. In these, audiometric examination revealed severe loss of hearing for high frequencies similar to that seen in cases of Rh iso-immunization cerebral palsy. In a further four, hearing ability has not yet been ascertained.

TABLE 1.

Royal Children's Hospital, Melbourne, 1958–1959; 606 Cerebral Palsy Cases (119 Premature Infants).

	Year of Birth.															
	1944	1945	1946	1947	1948	1949	1950	1951	1952	1953	1954	1955	1956	1957	1958	Total.
No history of jaundice:																
Not athetoid	2	4	1	4	3	4	4	9	14	3	4	10	6	5	4	77
Athetoid	—	—	1	—	1	—	—	1	1	—	2	1	2	1	—	10
History of jaundice:																
Not athetoid	—	—	1	—	—	—	—	2	1	—	2	1	—	—	—	7
Athetoid	—	—	—	—	—	—	—	1	—	3	6	9	4	1	1	25
Total	2	4	3	4	4	4	4	13	16	6	14	21	12	7	5	119
For comparison Rh-incompatible	1	1	—	4	4	3	1	5	5	4	1	4	1	5	2	41

Enamel defect in the deciduous teeth, which characteristically follows kernicterus, has been noted in six children, and in four more the teeth are doubtfully affected.

Speech has been late in developing, and virtually no useful speech has developed in 10. About nine should ultimately speak reasonably fluently. Educational prospects may be summarized as follows:

Attending normal school	3 children
Attending handicapped school	7 children
Expected to attend normal school	3 children
Expected to attend handicapped school	6 children
Expected to attend deaf school	3 children
Doubtful	3 children

This tabulation indicates a considerable burden on the special teaching facilities of the State.

The reason for increase in the incidence of kernicterus of prematurity is not easy to determine. It is hard to believe that the condition can have occurred in the past without being recognized, as the post-mortem features are so distinctive. It may be that there are more premature babies at risk since their survival rate has risen. This may be attributed to a greater interest in the care of premature infants over the last 10 years or so, to the introduction of antibiotics and to the development of modern electric incubators.

There seems to be some inverse correlation between the duration of gestation and the severity of the jaundice and the subsequent brain damage. This is summarized in Table VII. Similarly, birth weight appears to have some bearing. More mature and heavier babies are less often severely affected.

The pathology of kernicterus has provoked considerable interest, and at present the liver has been incriminated as the main site of the disturbance. It appears that indirect-reacting (to Ehrlich's diazo reagent) bilirubin alone is the toxic substance. After formation from breakdown of hæmoglobin, it is attached to serum albumin, apparently is lipid-soluble and can penetrate cells. Respiration of brain tissue is depressed *in vitro* by 20 mg. per 100 ml. of bilirubin. It has also been shown that bilirubin interferes with oxidative phosphorylation in brain cells in considerably lower concentrations than that required to depress cerebral oxidation. The bilirubin is converted into water-soluble direct-reacting bilirubin by conjugation with glucuronic acid by action of the enzyme glucuronyl transferase, which is present in the liver microsomes. The glucuronic acid is made available from uridine diphosphate glucuronic acid.

Functional immaturity of the glucuronyl transferase system has been demonstrated in various species. It is genetically defective in a strain of rats born jaundiced

TABLE II.

Twenty-five Jaundiced Premature Infants: Birth Details.

Case Number.[1]	Date of Birth.	Sex.	Weeks' Gestation.	Birth Weight. (Kg.)	Presentation.	Labour.	Delivery.	Onset of Respiration.	Condition at Birth.
1 (*a*)	5/ 7/51	F.	33	2·12	Vertex.	Spontaneous.	Normal.	2 min.	Satisfactory.
2	7/ 3/53	M.	28	1·11	——	——	——	——	——
3	26/ 3/53	M.	32	1·81	——	——	——	——	Satisfactory.
4 (*a*)	19/ 8/53	F.	32	1·67	——	——	——	——	——
5 (*a*)	5/ 5/54	F.	31	—	——	——	——	——	——
6	8/ 6/54	M.	35	2·95	——	Spontaneous.	Normal.	——	Satisfactory.
7 (*a*)	27/ 8/54	F.	35	2·15	——	Spontaneous.	Normal.	Immediate.	——
8	8/11/54	F.	35	1·59	——	Ante - partum hæmorrhage.	——	——	——
9	18/11/54	M.	35	2·44	Vertex.	Spontaneous.	Normal.	——	Asphyxia.
10 (*a*)	10/12/54	F.	30	1·33	——	——	Normal.	——	——
11	22/ 1/55	F.	35	1·76	——	Spontaneous.	——	——	——
12	1/ 2/55	F.	34	2·80	——	——	Normal.	——	——
13 (*a*)	10/ 2/55	M.	32	1·59	——	——	——	——	——
14	21/ 2/55	M.	32	1·81	——	——	——	——	——
15	2/ 3/55	F.	35	2·18	Vertex.	Ante - partum hæmorrhage.	Normal.	——	——
16 (*a*)	12/ 3/55	F.	36	2·12	——	——	——	——	——
17	12/ 5/55	M.	31	1·87	Vertex.	Spontaneous.	Normal.	Immediate.	Satisfactory.
18 (*a*)	9/ 6/55	M.	34	1·98	Vertex.	Spontaneous.	Normal.	Immediate.	Satisfactory.
19	2/ 7/55	M.	34	2·33	Vertex.	Induced.	Normal.	5 min.	Poor.
20	14/ 3/56	M.	34	2·11	Breech.	Spontaneous.	Forceps.	Immediate.	Satisfactory.
21 (*a*)	14/ 4/56	M.	28	1·53	Vertex.	Spontaneous.	Normal.	Delayed.	Poor.
22 (*a*)	3/ 5/56	F.	31	1·50	Breech.	Spontaneous.	Forceps.	Immediate.	Satisfactory.
23	16/ 6/56	M.	32	1·89	——	——	——	——	——
24 (*a*)	28/12/57	F.	32	1·59	Shoulder cord.	Spontaneous.	Cæsarean section.	Immediate.	Fair.
25	1/11/58	M.	32	2·09	Vertex.	Spontaneous.	Normal.	——	Satisfactory.

[1] (*a*), severely affected.

TABLE III.

Twenty-five Jaundiced Premature Infants: Neonatal Progress.

Case Number.	Jaundice.			Peak Serum Bilirubin Level.	Kernicterus Signs.	Cyanotic Attacks.	Exchange Transfusion.		Simple Transfusion. (Weeks.)	Streptomycin First Week.	Remarks.
	Day of Onset.	Duration.	Intensity.				Day.	Amount. (Ml.)			
1	5	Weeks.	Marked.	—	—	—	—	—	6	—	—
2	—	—	Marked.	—	—	—	—	—	3	—	—
3	2	12 days.	Marked.	—	—	—	—	—	—	—	—
4	3	—	Marked.	—	—	—	—	—	—	—	—
5	—	—	Marked.	—	—	—	—	—	—	—	—
6	2	7 days.	Moderate.	—	+	—	—	—	—	—	—
7	—	—	Moderate.	—	—	—	—	—	—	—	—
8	1	—	Severe.	—	—	—	—	—	—	—	—
9	3	11 days.	Marked.	—	Nil	++	—	—	—	—	—
10	—	—	Moderate.	—	—	—	—	—	—	—	—
11	2	—	Marked.	—	+	—	6	290	—	—	Rh-positive, mother Rh-negative, Coombs, negative.
12	2	—	Moderate.	—	—	—	—	—	—	—	—
13	3	—	Mild.	—	—	++	—	—	3	—	—
14	5	—	Marked.	—	+	—	5	120	—	—	—
15	—	—	Marked.	—	+	—	5	275	2	—	—
16	2	14 days.	Severe.	—	Nil	—	—	—	—	—	—
17	2	14 days.	Severe.	25 mg. per 100 ml.	+	—	4	380	2	80 mg. per day.	—
18	3	8 days.	Severe.	—	+	—	—	—	—	—	—
19	3	4 days.	Mild.	—	Nil	+	3	380	—	100 mg. per day.	—
20	1	9 days.	Mild.	19·1 mg. per 100 ml.	+	—	5	210	—	80 mg. per day.	—
21	1	10 days.	Marked.	—	Nil	—	—	—	—	—	—
22	5	8 days.	Marked.	19·5 mg. per 100 ml.	+	—	6	280	—	80 mg. per day.	—
23	—	—	Marked.	—	—	—	—	—	—	—	—
24	6	5 days.	Severe.	—	+	—	—	—	—	—	—
25	—	21 days.	Severe.	—	+	—	—	—	—	—	—

which subsequently develop kernicterus (Gunn, 1944). A similar genetically-determined congenital jaundice has been reported in an inbred family in West Maryland (Childs and Najjar, 1956; Crigler and Najjar, 1952). The majority of the survivors had clinical abnormalities characteristic of kernicterus. Although the enzyme system is immature at birth, this develops fully in full-term infants in about 10 days. With premature infants the immaturity of the system is more or less proportional to the immaturity of the baby.

Indirect-reacting bilirubin accumulates in the circulation as a result of failure of disposal once excretion through the placenta is cut off. With increasing concentrations, it passes the blood-brain barrier. This is said to occur more freely when the cerebro-spinal fluid protein concentration is raised, or if the serum albumin level is low (Harris *et alii*, 1958). It appears that premature infants may sustain neurological damage with serum levels of indirect-reacting bilirubin tolerated by maturely-born infants.

There is little satisfactory evidence that hæmolysis plays any part in kernicterus of prematurity, although it has been thought for many years that the change to an environment of high oxygen tension at birth did cause destruction of surplus red corpuscles. This hypothesis was based on animal experiments carried out by Goldbloom and Gottlieb (1929), in which animals were acclimatized to low oxygen pressures. On their return

TABLE IV.

Twenty-five Jaundiced Premature Infants: Present Physical State.

Case Number.	Cerebral Palsy.			Age in Months.		Mentality.[1]	Vision.	Hearing.	Tooth Defects.	Speech.	
	Athetosis.	Spasticity.	Ataxia.[1]	Sat Alone.[1]	Walked.[1]					Age of Onset. (Years.)	Quality.
1	Severe.	Moderate.	0.	—	—	Normal.	Normal.	Normal.	——	—	Nil.
2	Mild.	Moderate.	Marked.	10	42	Normal.	Normal.	Normal.	——	3	Good.
3	Moderate.	0.	0.	12	24	Normal.	Normal.	Normal.	?	3	Good.
4	Severe.	Severe.	0.	—	—	? Normal.	Normal.	Normal.	——	—	Some.
5	Severe.	Marked.	0.	—	—	?	Normal.	? Normal.	——	—	Nil.
6	Mild.	0.	Mild.	14	23	Normal.	Normal.	Normal.	?	2½	Good.
7	Marked.	Marked.	0.	—	—	Normal.	Normal.	Normal.	——	2	Good.
8	Moderate.	0.	Moderate.	13	24	Normal.	Normal.	?	——	2½	Fair.
9	Moderate.	0.	Mild.	—	33	Normal.	Normal.	Normal.	Ed.	3	Fair.
10	Marked.	Marked.	0.	—	—	Slow.	Normal.	Normal.	——	—	Nil.
11	Mild.	0.	0.	12	24	Slow.	Normal.	Normal.	——	2	Fair.
12	Mild.	0.	Moderate.	8	24	Normal.	Normal.	HFL ++[1]	?	—	Poor.
13	Severe.	Marked.	0.	—	—	? Normal	Normal.	Normal.	ED (green).	—	Nil.
14	Moderate.	0.	Mild.	15	30	Normal.	Normal.	Normal.	——	—	Nil.
15	Mild.	0.	Mild.	15	27	Normal.	Normal.	HFL +.	ED.	3	Fair.
16	Severe.	Marked.	0.	—	—	? Normal	Normal.	Normal.	ED.	—	Nil.
17	Mild.	0.	0.	9	22	Normal.	Normal.	HFL ++.	——	—	Nil.
18	Severe.	Marked.	0.	—	—	?	Normal.	? Normal	——	3½	Poor.
19	Mild.	0.	Mild.	—	25	Normal.	Normal.	Normal.	——	2	Normal.
20	Mild.	0.	Mild.	—	18	Normal.	Normal.	HFL ++.	——	3	Poor.
21	Marked.	Marked.	0.	48	—	Slow.	Normal.	Normal.	ED.	3½	Poor.
22	Marked.	Severe.	0.	—	—	Fair.	Poor.	?	——	—	Nil.
23	Moderate.	0.	Mild.	15	30	Normal.	Normal.	Normal.	——	3	Fair.
24	Marked.	Marked.	0.	—	—	Fair.	Normal.	? Deaf.	ED.	—	Nil.
25	Moderate.	0.	0.	—	—	Alert.	Normal.	?	?	—	Clear.

[1] "0", none present; "ED", enamel defect; "—", not yet achieved; "?", doubtful; "HFL", high-frequency loss.

to a normal oxygen tension, red-cell destruction and a rise in serum bilirubin concentration were demonstrated. Red-cell destruction probably does occur in new-born infants at a rate greater than in adults, and this may be due to the presence of larger cells containing much hæmoglobin F, which are mechanically more fragile than mature red cells. Red-cell production rapidly falls after birth. Extramedullary hæmatopoiesis promptly disappears, and the percentage of erythroblasts in the marrow falls.

There is some evidence that exposure to high oxygen concentration may have a direct toxic effect on developing brain tissue, especially in premature babies. Retrolental fibroplasia is frequently associated with cerebral palsy (Ingram and Kerr, 1954).

TABLE V.
Degree of Physical Defect.

Year of Birth.	Physical Defect.	
	Mild.	Severe.
1951	—	1
1953	2	1
1954	3	3
1955	6	3
1956	2	2
1957	—	1
1958	1	—
Total ..	14	11

TABLE VI.
Depth of Jaundice Related to Neurological Defects.
Table VIA.

Clinical Estimate of Depth of Jaundice.	Defects.	
	Mild.	Severe.
Mild	2	1
Moderate ..	2	2
Marked	7	5
Severe	3	3
Total ..	14	11

Table VIB.

Clinical Kernicterus	Defects.	
	Mild.	Severe.
Present	6	4
Absent	2	2
Not stated ..	6	5

Antibiotics administered in the neonatal period may aggravate the development of kernicterus. Sulphasuxazole has been shown to be harmful. Of four patients in this series who were given streptomycin in a dosage of 80 mg. or more per day for the first week of life, two subsequently had hearing defects, and one other may be deaf.

Vitamin K analogues in total doses over 30 mg. have been shown to cause hæmolysis and increase the risk of kernicterus (Crosse, Meyer and Gerrard, 1955).

Late ligation of the cord may increase the blood volume by up to 100 ml. This provides more hæmoglobin for breakdown to bilirubin.

Measures which have been introduced in an attempt to improve conjugation and excretion of bilirubin include the administration of glucuronic acid, exposure to blue fluorescent light and administration of thyroid hormones. Apparently glucuronic acid is in adequate supply, and extra may even be harmful. There is some doubt about the toxicity of substances produced in new-born infants by exposure to light, and the idea has been discarded. Thyroid hormones do increase the activity of glucuronyl transferase in new-born liver cells — this is probably by a promotion of all metabolic sequences in the cell. In premature infants given triiodothyronine, Lees and Ruthven (1959) demonstrated a statistically significant reduction of bilirubin concentration, and the peak concentration occurs earlier. However, the degree of reduction of bilirubin would not materially help in therapy. At present the only satisfactory line of therapy is by exchange transfusion.

TABLE VII.
Twenty-five Jaundiced Premature Infants.

Prematurity and Birth Weight.	Physical Defects.		
	Severe.	Mild.	Total.
32 weeks' gestation or less	7	6 (1 child deaf)	13
33 weeks' gestation or more	4	8 (3 children deaf)	12
Birth weight under 1500 grammes ..	2	1	3
Birth weight 1500 to 2000 grammes ..	6	6 (1 child deaf)	12
Birth weight over 2000 grammes	3	7 (3 children deaf)	10

The results in seven cases in which such transfusions have been given in this series are shown in Table VIII.

TABLE VIII.
Infants Given Exchange Transfusion.

Case Number.	Year of Birth.	Kern-icterus.	Peak Bilirubin Level.	Transfusion.		Final Defect.	Deaf-ness.
				Day.	Amount.		
11	1955	+	—	6	290 ml.	Mild.	—
14	1955	+	—	5	120 ml.	Mild.	—
15	1955	+	—	5	275 ml.	Mild.	+
17[1]	1955	+	25 mg. per 100 ml.	4	380 ml.	Mild.	++
19	1955	—	—	3	380 ml.	Mild.	—
20[1]	1956	+	19·1 mg. per 100 ml.	5	210 ml.	Mild.	++
22[1]	1956	+	19·5 mg. per 100 ml.	6	280 ml.	Severe.	?

[1] Streptomycin given, 80 mg. per day for first week.

The results are not satisfactory, in that neurological sequelæ have occurred; but perhaps it is consoling that only one patient is severely affected physically. These transfusions were given late, and when clinical evidence of kernicterus was already present in all but one case, but it is contended that they considerably reduced the degree of cerebral damage.

Management of jaundice of prematurity depends on the knowledge that the condition is potentially dangerous, if not fatal. Once clinical signs of kernicterus have developed, it appears that neuron damage has occurred. All 16 survivors of 60 kernicteric premature babies reported by Crosse, Meyer and Gerrard (1955) had permanent neurological defects. It is held that neurological signs were present in the neonatal period in the 25 children of the present series more often than has been reported, and that these have been overlooked for want of adequate vigilance, in the mistaken belief that kernicterus occurs only in hæmolytic disease. Clini-

cal evaluation of jaundice in the new-born is extremely unreliable, especially in a plethoric infant, and serum bilirubin estimations have hitherto often been misleading. However, they must form the basis of observation of developing hyperbilirubinæmia (Lucey, 1960).

To be fully effective, exchange transfusion should be given before neurological signs have appeared. The improved technique developed by Kitchen (1960) at the Royal Women's Hospital, Melbourne, shows great promise; greater removal of bilirubin is obtained by preliminary introduction of serum albumin. The contention recently proposed by Mores (1959), that exchange transfusion is of unproven value and that hyperbilirubinæmia in premature infants should be allowed to follow its natural course, cannot be supported.

Summary.

Twenty-five survivors showing neurological sequelæ of jaundice of prematurity are described. These children are similar to those who survive kernicterus due to Rh-factor iso-immunization.

Management of jaundice of prematurity consists of early recognition and prompt treatment by exchange transfusion if there is any threat of kernicterus.

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ALCOHOL, COLLISIONS AND PREVENTIVE MEDICINE.

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1000 Australian lives might be saved each year if motorists could be persuaded not to drink before they drove their cars.

DR. L. G. NORMAN, Chief Medical Officer of the London Transport Executive, made the foregoing statement in *The Age*, Melbourne, on October 24, 1959.

The principles of preventive medicine should be applied to the problem of alcoholism and road accidents. An attempt was made to apply these principles during the Latrobe Valley Safety Town Campaign. This attempt is described in order to present the results, to outline the difficulties in applying the principles and to stimulate further action in this field.

Accidents kill about 5000 Australians each year. About half of these deaths result from traffic collisions. Recent evidence ("Medical Guide", 1959; Pearson, 1957; Birrell, 1960) suggests that about half of these collisions are associated with the presence of significant amounts of alcohol in the blood of the drivers. Therefore, probably 1000 Australian lives are lost each year through traffic collisions involving motorists who drank before they drove their cars. These lives are 1000 good reasons for attempting to persuade all motorists not to drink before they drive their cars.

For several years I have been chairman of the Morwell Branch of the National Safety Council of Australia. This branch conducted Australia's first Safety Town Campaign in 1957-1958. I believe that prevention should be more effective than mere treatment in reducing the morbidity and mortality of collisions. Preventive medicine is a part of almost every doctor's practice. We use it to limit the onset and progress of most diseases. I therefore tried to apply an epidemiological approach to the problems of local traffic collisions. Gordon (1949) and Press (1948) list four steps in this approach; (i) determine the problem; (ii) establish the causes; (iii) develop specific preventive measures to control the causes; (iv) evaluate the results.

The Problem.

Definitions.

The word "accident" has been defined as a sudden, unexpected occurrence usually resulting in injury. Many accidents are neither sudden nor unexpected, nor do all result in injury. "Collision" is used here as a term for a sudden, violent contact of a motor-vehicle with another object resulting in human injury. Injury-producing collisions should be, but are not always, reported to the police. "Under the influence of alcohol" could cover any person with a blood-alcohol level above zero. I considered it "significant" if the motorist had had more than four beers shortly before driving, if he appeared visibly affected by alcohol as judged by witnesses, the police or myself, or if he had a blood-alcohol level above 0·05%. (Report of B.M.A. Committee, 1960; Editorial, 1960.) The present inadequate definitions and reporting lead to confusion and inability to determine the problems accurately and to assess and compare results. The Road Safety movement should urgently establish standard definitions and reporting procedures.

Investigation of Local Collisions.

I soon realized that scientific investigation and statistical analysis of local collisions would be impossible. Not all collisions were reported, nor could all be investigated. Information was often hearsay, incomplete, misleading or forgotten. Some was privileged, and some could lead to our being involved as witnesses in subsequent litigation. The information came from the victims, police, witnesses, ambulance officers, tow-truck operators and panel-beaters. I also inspected the vehicles, the occupants and the collision sites on many occasions. From such information, no definite conclusions can be made regarding the exact causes of any particular collision. There is a need for scientific research into these causes by some competent body.

Findings.

About 100 collisions with five deaths had been occurring each year within a four-mile radius of Morwell, with a maximum of nine deaths in 1956-1957. During the Safety Town Year, this figure dropped to 75 collisions with two deaths, and the following year the figures were 95 and three respectively. Alcohol was

smelt, seen or spoken of in three-quarters of the collisions, over half the vehicles were reported as returning from hotels or parties, Saturday was the worst night, the Prince's Highway the worst road, and local drivers were mostly involved, the majority being young, working-class males. Of the blood-alcohol tests taken for the police, with one exception of 0·11%, all the levels were over 0·22%. Not all these drivers were convicted. Alcohol was not officially blamed in coroners' findings on any traffic deaths; yet clinical histories and examinations and several post-mortem blood tests indicated that alcohol was significant in 14 out of 19 consecutive traffic deaths in this area.

Effects of Alcohol on Driving Ability.

Small amounts of alcohol can impair driving ability. Tolerance to glare, fields of vision and the senses of caution and judgement can be affected at 0·03% or by as few as three seven-ounce glasses of beer with a 5% alcohol content ("Medical Guide", 1959). These affected faculties are all essential in driving a car. Impairment of these and other faculties increases with rising blood-alcohol levels. At over 0·10%, motorists' chances of being involved in a collision are significantly increased (Report of B.M.A. Committee, 1960).

Establishment of Causes.

It is difficult to prove that impairment of driving ability by alcohol is the sole cause of any particular collision. Collisions, in fact all "accidents", rarely have a single cause. Usually a combination of contributory factors in man and his environment leads to a disease or an "accident". Elimination or modification of these factors so as to avoid disease, disability or death is the function of preventive medicine. The high degree of association of local collisions with a motorist who had been drinking alcohol before he drove his car has given me the very strong impression that alcohol has been a major factor contributing to these collisions.

Development of Specific Preventive Measures

Destruction of the Agent.

The abolition of alcohol was considered to be impossible.

Increasing Man's Resistance.

Resistance or tolerance to alcohol is said to develop after continued, heavy drinking (Council on Food and Nutrition, 1959). This sort of resistance can hardly be considered desirable. Increasing man's resistance to collisions by the development of safer vehicles is worthy of urgent attention, but could not be achieved by our campaign.

Protection by Interrupting the Combination of Contributory Factors.

This appeared to offer some measure of control. Persuading motorists not to drink at all was also considered to be impossible. We avoided a temperance campaign. We tried to interrupt the combination of motorists drinking alcohol and then driving their cars. Persuading motorists not to drink before they drove their cars was considered to be a form of health education. The Safety Council Branch was supported in such a programme by the doctors and clergy of Morwell in November, 1959. We tried to teach the following: (i) the effects of alcohol on driving ability; (ii) alcohol's contribution to three-quarters of Morwell's collisions; (iii) the need to leave the car at home and use a taxi, bus or non-drinking driver when going to an hotel or a party; (iv) the fear of being involved in a collision or being caught by the police, who cooperated by concentrating upon drinking drivers that month. We made use of leaflets, posters, talks and Press articles.

Evaluation of Results.

Here again we lacked specific information before and after the campaign, and this precluded statistical proof. The techniques we used were neither difficult nor expensive, but did require much man-power. Support for the campaign and the subsequent drinking driver programme was readily forthcoming. The police have reported improvements in driving behaviour. My medical colleagues in Morwell have remarked how much quieter are their Saturday nights on call since the campaign began. Yardsticks for measuring the success of such programmes are not available, but the Safety Town Campaign, with all its activities, has resulted in a reduction of the collision and traffic-death rates in Morwell. Deaths from collisions associated with alcohol have fallen in the past four years from seven one year to two, then one, and now none for the past 12 months.

TABLE I.

Attempts to Assess the Effects of Consumption of Small Amounts of Alcohol.[1]

Subject.	Bottles of Beer Consumed.	Approximate Blood-Alcohol Level.[2]
A	0	Zero
B	1	0·04%
C	2	0·08%
D	3	0·12%
E	4	0·16%

[1] Order of placement: correct, A B C D E; Rotary, D C B E A; Chamber of Commerce, E C D B A.

[2] One bottle contains 26 oz. of beer with an alcohol content of 5%. The subjects consumed the beer rapidly on empty stomachs and were tested one hour later. They were examined by members of the organizations mentioned above, who were asked to place them in an order corresponding with the amount of alcohol consumed.

Further Applications of Preventive Medicine.

Instead of the present attitude of waiting for collisions to occur and then treating the injuries, the following measures have been tried and are recommended to other doctors: (i) investigating local collisions for information, not only of use in treating the injuries, but also of use in helping to prevent further similar collisions; (ii) giving personal advice to patients who are inclined to "drive under the influence"; (iii) responding to the civic duty of examining drinking drivers when requested by the police, and applying the methods outlined in the B.M.A. publication "Recognition of Intoxication"; (iv) establishing, leading or assisting local safety councils, especially in their efforts to persuade motorists not to drink before they drive; (v) above all, setting a good example to the rest of the community by not drinking before driving.

Discussion.

There is an increasing demand that "somebody should do something" about the problem of traffic collisions. Many editorials, letters to the editor and Press articles are demanding that the Government should do something. Certainly, better legislation is needed to make it easier for police to prosecute successfully those who drive when their ability is impaired by alcohol. I have found that there is no satisfactory prosecution of those who drive with blood-alcohol levels between 0·05% and 0·20% (Report of B.M.A. Committee, 1960). These drivers are likely to be a menace on the road, but may not appear to be visibly affected. To emphasize this difficulty, we arranged a demonstration. Volunteers drank differing amounts of beer and were tested by members of Rotary and the Chamber of Commerce about an hour later. The volunteers were then to be placed in a line in an order corresponding to the numbers of bottles of beer they had drunk. The results (Table I) indicate the difficulty of detecting by superficial observation those with small but significant blood-alcohol levels. The police tested one subject who had drunk four bottles of beer. He was able to pass the police tests and would not have been arrested had he been caught driving. Even

clinical examination by doctors cannot detect these lower levels accurately. Therefore, some chemical tests are needed, whether voluntary or compulsory (Committee of Medicolegal Problems, 1959).

Enforcement of adequate legislation is just one way of persuading motorists not to drink before they drive. Education to persuade motorists must be developed according to the principles of health education (Leavell and Clark, 1958). The Safety Town Campaign was an experiment in developing such educational techniques. Further experience in future campaigns will find more effective techniques. Education will then replace enforcement as our main method of control of this major medical problem.

Conclusions.

As a result of experience gained as chairman of the Latrobe Valley Safety Town Campaign, it is my impression that the impairment of driving ability by alcohol is a major factor contributing to at least half the mortality and morbidity of traffic collisions. Scientific investigations are needed before this impression can be confirmed. The epidemiological principles of preventive medicine can be applied to achieve some measure of control of this problem. Persuading motorists not to drink before they drive their cars is suggested as a practical means of control. The methods used in such an attempt are a form of Health Education (Editorial, 1959). The medical profession, individually and collectively, should accept the responsibility for leadership in campaigns for the control of this problem, a problem which accounts for much death and disability, and which, to date, has been virtually ignored.

Summary.

About 1000 Australian lives are lost each year in collisions in which alcohol is a major contributing factor.

The epidemiological principles of preventive medicine have been applied to this problem during and since the Latrobe Valley Safety Town Campaign.

The application of these principles is described.

The results indicate that this problem can be controlled.

Acknowledgements.

I should like to record my appreciation of the work done in this field of preventive medicine by Dr. John Birrell, Victoria Police Surgeon, Dr. F. S. Hansman, of Sydney, and Dr. R. Englebrecht, Chairman of the Cooma Safety Town Campaign. I also thank Mr. Ian Malloch, Manager of the National Safety Council of Australia, and Dr. Birrell for their encouragement and assistance.

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PERFORMANCE OF THE "C.I.G." TWO-CANISTER CARBON-DIOXIDE ABSORBER.

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WE in Melbourne were first introduced to the idea of the two-canister carbon-dioxide absorber in 1959, when Professor Lucien Morris, who was then visiting Australia spoke in its favour. More recently Dr. J. Adriani and Dr. G. Miles, of New Orleans, have described the performances of various American two-canister absorbers.

The present paper deals with tests carried out at the Royal Melbourne Hospital on the two-canister absorber manufactured by the Commonwealth Industrial Gases Co. of Australia (Figure I). The photograph is largely self-explanatory. The corrugated hoses have been removed to allow a better view of the apparatus. The patient exhales through the canister on the right of the picture into the rebreathing bag, and inhales through the canister on the left side. This arrangement equalizes the resistance to respiration during both inspiration and expiration. In conformity with accepted practice, the oncoming new gases are added on the inspiratory side of the apparatus, and the valve for the overflow of excess gases is located on the expiratory side.

The tests were carried out on adult patients. In order to evaluate the apparatus under conditions of everyday use, the anæsthetic agent was added to a flow of gases consisting of 1 litre of oxygen and 2 litres of nitrous oxide per minute. Naturally the overflow of excess gases would carry a proportion of carbon dioxide with it, and therefore somewhat extend the life of the soda lime. This was intentional and understood, as the aim was to test the apparatus under clinical conditions. Carbon-dioxide estimations were made with the Liston-Becker infra-red analyser. Three different brands of soda lime were used.

The apparatus was tested with regard to both carbon dioxide absorption and resistance to respiration.

Carbon-Dioxide Absorption.

The two-canister absorber was found to be very effective in removing carbon dioxide. When two canisters, each containing 1 lb. of 6–8 mesh soda lime, were used, no carbon dioxide measurable with the Liston-Becker analyser appeared in the gases to be inhaled for periods of 15 hours, 15 hours and 18 hours respectively with the three different brands. A concentration of 0·5% (which figure has been accepted by Dr. Adriani and Dr. Miles as an arbitrary one indicating failure of the soda lime from a clinical point of view) was reached at 21 hours, 21 hours and 24·5 hours respectively.

Examination of the soda lime at this time showed extreme colour change in the first canister and a gradation of colour change in the second canister ending with soda lime of unchanged colour.

Resistance to Respiration.

A water manometer was connected by a length of rubber tubing to a point near the face-piece. It was found that in a patient anæsthetized to light Stage III depth of anæsthesia, the pressures developed were approximately +0·75 cm. to −0·75 cm. of water. These low pressure changes would be possible only if the resistance to respiration was small.

Discussion.

In the practice of anæsthesia, it is customary to regard soda lime as being exhausted when it permits 0·5% of carbon dioxide to pass into the inhaled gases. However, from a chemical point of view this soda lime is still quite active and able to absorb further carbon dioxide. In the two-canister absorber, this remaining carbon-dioxide absorp-

tive power in the soda lime of the first canister is utilized, and it is this greater exhaustion of the soda lime in the first canister that enables the two-canister absorber, when freshly charged, to have four times the life of a single canister instead of only twice, as one at first sight might have expected.

The effective removal of carbon dioxide for an average of 16 hours, plus the low resistance of the apparatus, makes it possible to use the adult-size circle absorber on

FIGURE I.

The C.I.G. two-canister absorber. The corrugated hoses have been removed so as not to obscure the view of the apparatus.

quite small children, which was not possible with single canister absorbers.

As soda lime is one of the cheapest commodities used by anæsthetists, one would not gain much financially by economizing in it. However, the significant factor is the much greater period of completely effective carbon-dioxide absorption, and it is this which justifies the use of the two-canister absorber.

If one is to make full use of the soda lime without running the risk of excessive exhaustion, then one must mark off the hours of use carefully. In public hospital practice, in which many anæsthetists may use one machine, this is frequently forgotten. Under such circumstances it would appear that the only safe method would be to discard the soda lime as a routine measure at a time when it is still a good way from being spent. The use of transparent canisters may provide an answer to this problem.

Under clinical conditions, one would have to use the soda lime on from ten to twenty different patients if one was to obtain full use from it. Experience suggests that the risk of infecting patients from anæsthetic equipment is not great; but if one anæsthetizes a patient with an infective respiratory tract disease, it would appear likely that the soda lime will be contaminated. In this connexion, the possibility of steam sterilization of the canisters containing soda lime in an instrument autoclave was tested. It was found that the soda lime granules did not disintegrate, and that the ability to absorb carbon dioxide appeared unaltered. However, the heated canisters took about half an hour to cool, so that sterilization of soda lime between cases would not be feasible.

Conclusions.

The "C.I.G." two-canister absorber, when used with flows of 1 litre of oxygen and two litres of nitrous oxide per minute, was found to remove carbon dioxide effectively from exhaled gases, so that measurable quantities in the inhaled gases did not appear for an average of 16 hours. Clinical exhaustion of the soda lime as shown by the appearance of 0·5% of carbon dioxide in the inhaled gases occurred in an average of 22 hours. Thus the two-canister absorber was about four times as effective as the single canister absorber.

Resistance to respiration was low, as demonstrated by measurement of pressure changes near the face-piece.

Acknowledgement.

The photograph of the "C.I.G." two-canister absorber was taken by the Photographic Department of the Royal Victorian Eye and Ear Hospital.

Reference.

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CARCINOID SYNDROME RESULTING FROM A MALIGNANT ARGENTAFFINOMA IN A MECKEL'S DIVERTICULUM.

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IT is now generally agreed that argentaffinomas arise from the Kultschitzky cells of the crypts of Lieberkuhn and hence may arise from any part of the gastro-intestinal tract. The first adequate description of the tumour was given in 1888 by Lubarsch. Oberndorfer in 1907 coined the word "carcinoid", and although an association of valvular heart disease with metastasizing carcinoid tumour was noted by Cassidy in 1930 and 1934, it was not until 1953 that three groups of workers (Thorson, Biorch and Bjorkman; Isler and Hedinger and Rosenbaum; Santer and Clandon) independently described the carcinoid syndrome.

The components of this syndrome, resulting from excessive secretion of 5-hydroxytryptamine (serotonin) are transient and permanent vasomotor phenomena, intestinal hyperperistalsis, bronchoconstriction, œdema, ascites, pellagra-like skin lesions and right-sided subendocardial sclerosis with signs of pulmonary and tricuspid valvular disease.

The association of carcinoid syndrome with a malignant argentaffinoma arising in a Meckel's diverticulum has hitherto never been described. There have been, however, 14 cases of argentaffinoma in Meckel's diverticula reported in the literature, the first by Hicks and Kadinsky in 1922 and the most recent by Baird, Anderson and Mills in 1958. The latter authors reviewed all the cases and noted that although invasiveness was a frequent finding, only one of these tumours had metastasized.

The case to be described is, as far as we are aware, unique, in that the foregoing syndrome accompanied a malignant metastasizing tumour of a Meckel's diverticulum.

Clinical Record.

A female patient, aged 60 years, was admitted to the Royal Adelaide Hospital in 1959 with a history of inter-

mittent diarrhœa of 18 months' duration. The diarrhœa, which lasted for two to three days with equal periods of remission, had dated from a surgical repair of a ventral hernia. Investigations for an alimentary neoplasm were undertaken in 1958, but gave negative

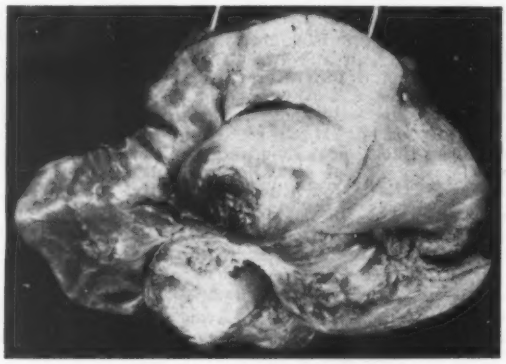


FIGURE I.
The Meckel's diverticulum partly inverted, and distorted by an infiltrated mass of mesenteric glands.

results. Three months prior to her admission to hospital, shortness of breath had been noted on mild exertion, with swelling of ankles and weight loss. At this time indefinite abdominal pain had been associated with the diarrhœa, which had become profuse, with blood and/or mucus appearing constantly in the stools.

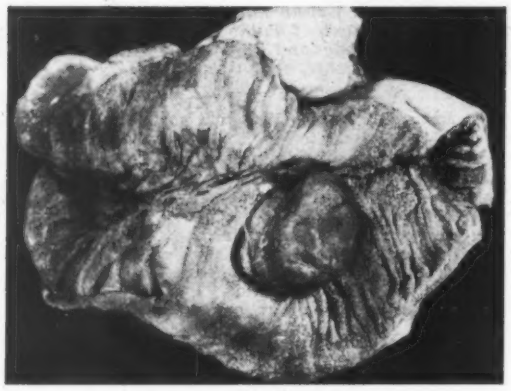


FIGURE II.
The tumour prolapsing into the lumen of the terminal portion of the ileum.

On examination, the patient was depressed. Flushing of the face and neck, and cyanosis of the lips and fingers with dilated venules on the cheeks were noted. Examination of the cardio-vascular system revealed a basal diastolic bruit, a systolic bruit maximal along the left border of the sternum, normal peripheral pulses, a blood pressure of 130/70 mm. of mercury and œdema of both ankles, but clear lung bases. A liver enlarged to two fingers' breadth below the right costal margin was palpated, as well as an indefinite epigastric mass. Investigations gave the following results: the blood, barium enema X-ray findings, fæcal smears and cultures and serum electrolyte estimations were normal. The total serum protein content was slightly reduced. Persistent oliguria (a daily output of 9 to 10 oz. despite adequate fluid intake) was noted.

Ulcerative colitis was a favoured diagnosis, and treatment with ACTH, astringent mixtures and a protein-rich diet was instituted. Before further investigations could be made the patient died suddenly.

Autopsy.

The autopsy revealed a polypoid tumour arising in a distorted Meckel's diverticulum (Figures I and II). There was evidence of strangulation and bleeding from

FIGURE III.
The tricuspid valve viewed from the ventricular aspect.

the tumour resulting from partial inversion of the diverticulum. Mesenteric glandular metastases had caused adhesions between proximal and distal loops of ileum to form an irregular mass, which had been palpated during life. Massive metastatic deposits were found in the liver, and there was a single small deposit in the subpleura of the lower lobe of the right lung.

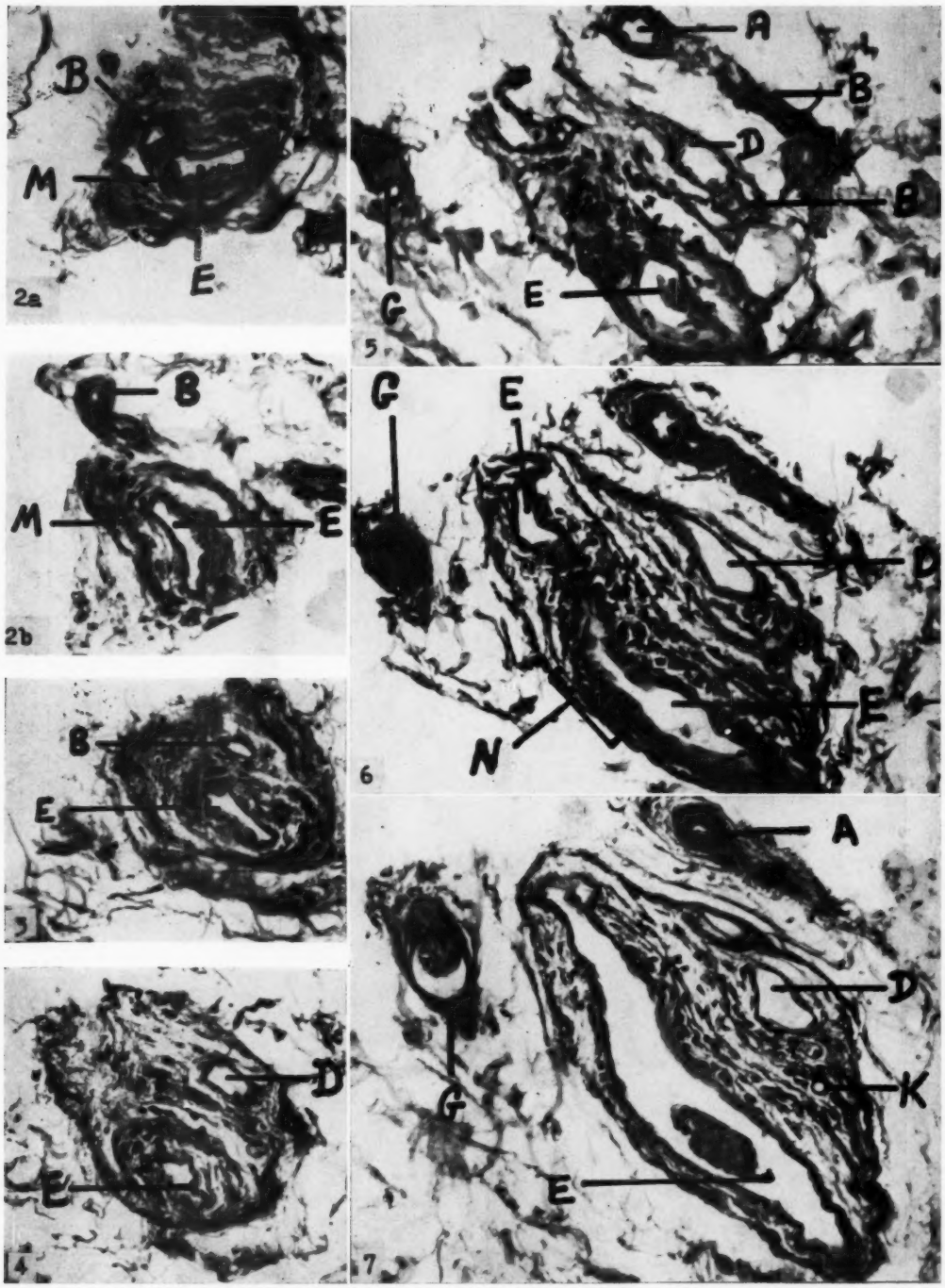
The heart showed gross stenosis of the pulmonary and tricuspid valves (Figure III), which admitted only the tip of the index finger. The valve rings were sclerosed and the commissures obliterated. The valve margins were thickened, distorted and partly fused together, forming incompetent diaphragms. The tips of the tricuspid papillary muscles and the chordæ tendineæ were shortened, scarred and distorted.

The brain and kidneys were normal.

Microscopic examination showed that the primary tumour was a typical infiltrating carcinoid (Figure IV[1]), with cords, nests and pseudorosettes composed of uniform round or polyhedral cells suspended in a fine connective tissue matrix. These cells had plentiful eosinophilic cytoplasm with dense, well-demarcated nuclei. Mitotic figures were rare. Although cytoplasmic granules were not seen with hæmatoxylin and eosin or fast red diazo stains, Fontana silver preparations revealed a fine, dust-like cytoplasmic granularity (Figure V).

[1] For Figures IV to VI see art-paper supplement.

ILLUSTRATIONS TO THE ARTICLE BY C. J. GRIFFIN.



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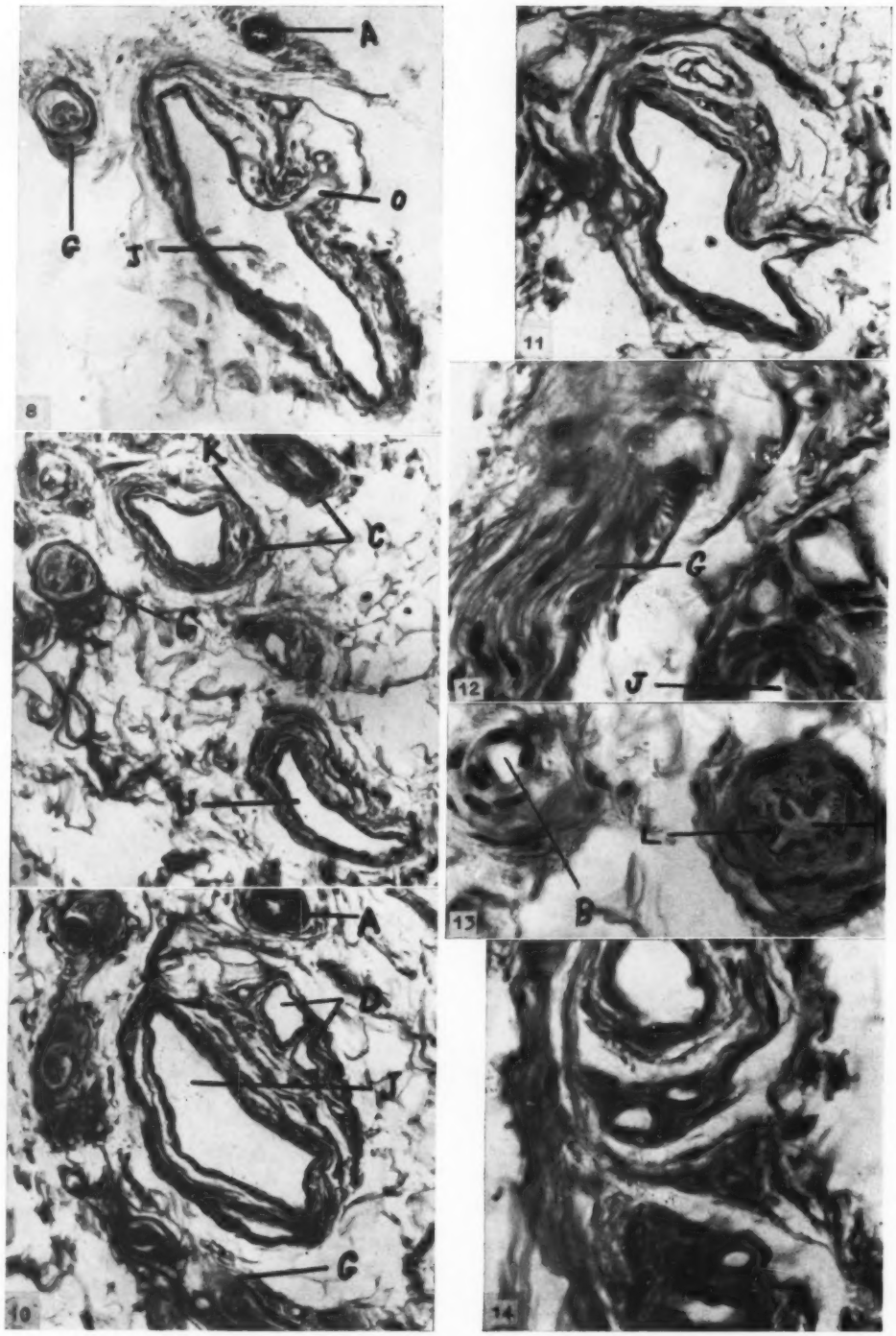

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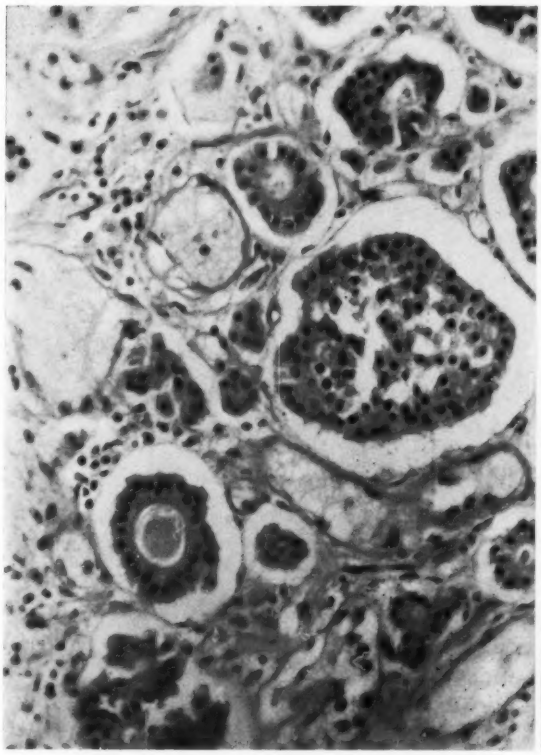

FIGURE IV.
The primary tumour (× 40).

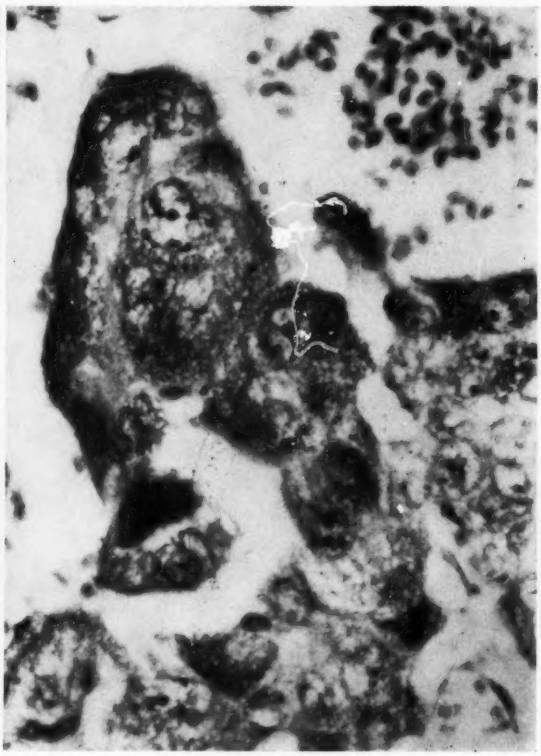

FIGURE V.
The primary tumour (Fontana silver stain, × 400).

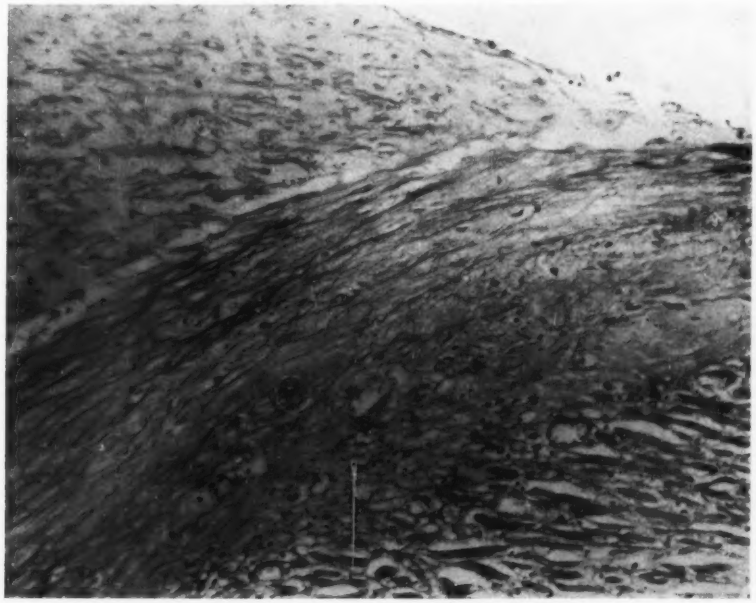

FIGURE VI.
The sclerosed pulmonary trunk (Verhoeff and Van Gieson stain, × 40).

ILLUSTRATIONS TO THE ARTICLE BY B. RYAN.

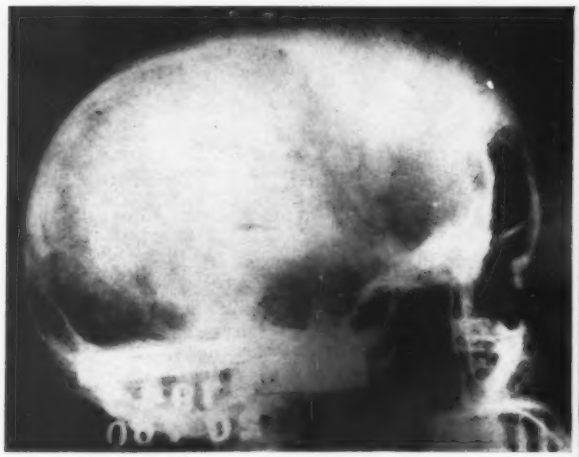

FIGURE I.

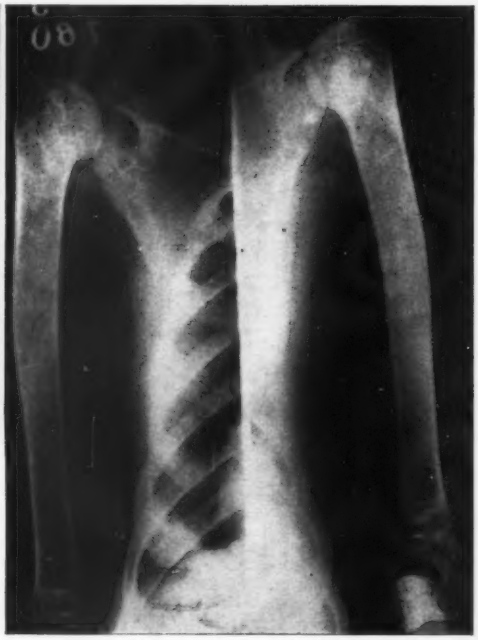

FIGURE II.

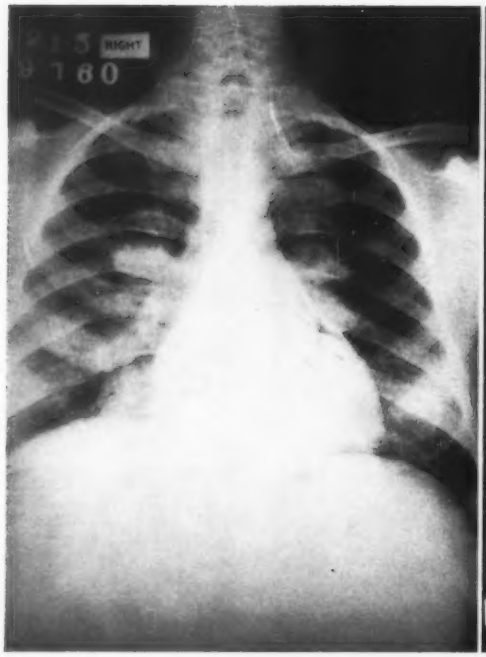

FIGURE III.

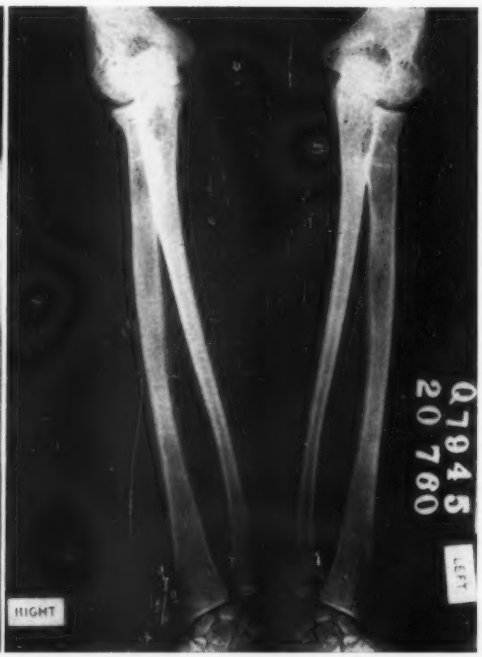

FIGURE IV.

Microscopic examination of the pulmonary trunk showed an intact endothelium lying on a thick band of loose, fibroblastic connective tissue, with increasing collagen density towards the myocardium (Figure VI). In the deeper layers of this plaque, Verhoeff and Van

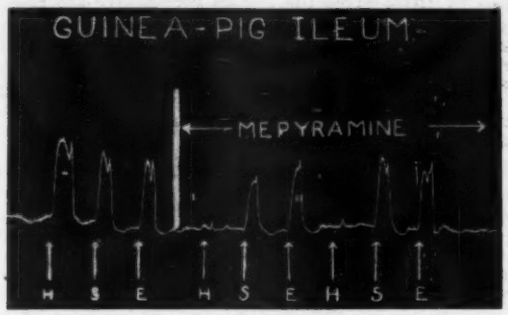

FIGURE VII.
E, 0·2 ml. extract of tumour × 80; S, serotonin 2·0 μg.; H, histamine 0·5 μg.

Gieson stain showed an irregular reduplication of elastic fibres. In this zone there was a sparse infiltration by lymphocytes and occasional plasma cells, while diffuse interstitial fibrosis was noted in the subendocardial muscle layer. These cardiac lesions agree with the detailed descriptions given by Thorson in 1958.

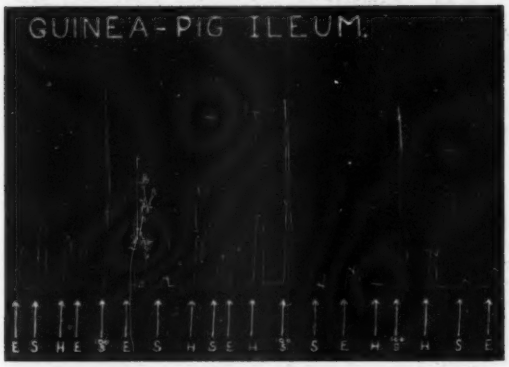

FIGURE VIII.
H, histamine 0·5 μg.; S, serotonin 1·0 μg.; E, 0·2 ml. extract of tumour × 80; mepyramine maleate 10·0 μg.

Assay of Serotonin.

An extract of the tumour was prepared by homogenizing 25 grammes of liver metastasis in 100 ml. of a M/100 hydrochloric acid solution containing sodium dihydrogenphosphate (M/200) and ascorbic acid (M/2000). The mixture was centrifuged at 4° C., and the superatant frozen. Portions were thawed, diluted twentyfold and neutralized for assay purposes when required.

Preliminary tests revealed that the extract produced spasm of the rat uterus and guinea-pig ileum, and the probable identification of the active principle with serotonin was indicated by the following tests:

1. Serotonin in high concentrations desensitizes the guinea-pig ileum to the stimulant action of low concentrations of serotonin, but does not affect the response to other smooth-muscle stimulants such as histamine and acetylcholine (Gaddum, 1957). Figure VII shows that guinea-pig ileum was desensitized by prior treatment with serotonin to the extract and to serotonin, but not to acetylcholine or histamine.

2. The stimulant actions of the extracts on the guinea-pig ileum and rat colon were unaffected by antagonists of histamine (mepyramine maleate), but were abolished by an antagonist of serotonin (B.O.L., bromlysergic acid diethylamide). The antagonistic effect of B.O.L. was restricted to the rat colon (Figures VIII and IX). Responses to acetylcholine were unaffected by B.O.L.

3. The extract and serotonin produced identical effects on the blood pressure of the anæsthetized rat. These effects comprised an initial transient increase followed by a more prolonged decrease in blood pressure. After ganglionic blockage, the pressor effect was accentuated

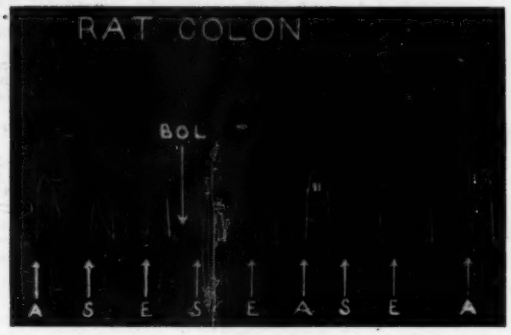

FIGURE IX.
A, acetylcholine 0·5 μg.; S, serotonin 1·0 μg.; E, 0·1 ml. extract of tumour × 80; B.O.L., 10 μg. bromlysergic acid diethylamide.

while the depressor effect was abolished. In each of the foregoing tests, serotonin and the extract behaved in an identical fashion, and it was estimated that the tumour contained 0·8 mg. of serotonin per gramme of fresh weight of tissue.

4. Chromatographic analysis was carried out by the method of Curzon (1955); 0·04 ml. quantities of the undiluted extract and the undiluted extract plus 250 μg. of serotonin per millilitre were compared. The colour changes to *p*-dimethyl amino-benzaldehyde were identical with those described by Curzon, and were restricted to one region of the paper in each case. The Rf values were identical.

On the basis of the foregoing tests, it was concluded that the tumour contained serotonin in amounts of at least 0·8 mg. per gramme of tissue. The contents of serotonin in carcinoid tumours described in the literature range from 0·58 to 2·5 mg. per gramme (Collier, 1957).

Discussion.

Despite the incidence of Meckel's diverticulum in 2% to 3% of autopsy examinations, malignant tumours of this vestigial remnant are very rare. Benign, infiltrating and metastasizing argentaffinomas have previously been described arising in this viscus, but we believe this is the first report of a malignant metastasizing carcinoid tumour associated with the classical carcinoid syndrome.

This case demonstrates that the characteristics of these tumours in this site are in no way different from argentaffinomas arising in the more common situations.

Acknowledgements.

We are grateful to Miss F. Vogt and Miss M. E. Gladstone for histological work, to Miss M. Dopson for the photography, to Dr. R. Britten Jones for permission to publish this case and to Professor R. F. Whelan for advice and criticism.

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Reports of Cases.

THALASSÆMIA: REPORT OF A CASE IN PAPUA.

By B. RYAN, M.B., B.S. (Melb.), M.R.C.P. (Edin.), D.G.O., D.C.H.,
Medical Officer, Grade II.
From the General Hospital, Taurama, Port Moresby.

THALASSÆMIA, also known as Mediterranean anæmia and Cooley's anæmia, was first described by Cooley and Lee (1925, 1932) in "children with splenomegaly, anæmia and peculiar bone changes". It was at first thought to be usually fatal in childhood; but it was later recognized that this is not invariably so and the disease was subdivided into major and minor forms. In 1955, Sturgeon *et alii* described types intermediate between major and minor forms. It is now considered that the major form of the disease represents a homozygous state and the minor form a heterozygous state (Valentine and Neel, 1944).

The disease was at first thought to be confined to Mediterranean races, but is now known to occur in Africa and various parts of Asia, being particularly prevalent in Thailand. It is also known to occur in Indonesia, but has not previously been reported in New Guinea.

Thalassæmia is associated with three abnormalities of hæmoglobin synthesis—the presence of fœtal hæmoglobin, the suppression of adult hæmoglobin production, and an increase in hæmoglobin A_2. Fœtal hæmoglobin is found in heterozygotes as well as in homozygotes, but usually in much smaller amounts. In thalassæmia major the amount of fœtal hæmoglobin varies from less than 20% to more than 90%, whereas in heterozygotes it is commonly less than 4%. However, the amount of fœtal hæmoglobin present is not particularly related to the severity of the anæmia (Sturgeon *et alii*, 1955).

It has been known for nearly 100 years that the hæmoglobin of cord blood is more resistant to alkali denaturation than that of adult blood, and advantage is taken of this property to estimate quantitatively the amount of fœtal hæmoglobin present in a mixture of hæmoglobins. The method used in the case to be described is that devised by Singer *et alii* (1951).

It is known that adult hæmoglobin appears in the fœtus at 13 weeks and reaches 30% at 42 weeks, and that fœtal hæmoglobin is reduced to 10% at the fourth month of extrauterine life. Small percentages are present at two years in the normal child.

It is also known that different hæmoglobin molecules move at different rates in an electrical field, and that one of the best methods of distinguishing the presence of fœtal hæmoglobin is by starch gel electrophoresis, in which the hæmoglobin solution is made to migrate in a mass of starch.

Clinical Features of Thalassæmia Major.

Pallor, hepatomegaly and splenomegaly are usually the presenting signs, and often occur at an early age. Later there is "bossing" with enlargement of the skull, and the child develops a mongoloid appearance accompanied by retardation of growth. Jaundice is rare.

Radiological examination reveals widening of the diploë of the skull, and widening due to enlargement of the medulla of the long bones, with thinning of their cortices. The short bones, such as the metacarpals and metatarsals, often become rectangular in appearance, and trabeculation of the medulla gives rise to a mosaic appearance. These latter changes regress with age, while changes in the skull, spine and pelvic bones increase (Caffey, 1937). The bony changes are not directly related to the severity of the anæmia.

A hypochromic, microcytic anæmia is present, with anisocytosis and poikilocytosis, and target cells are prominent. Normoblasts are almost invariably present. The reticulocyte count is usually moderately increased and the leucocyte counts are usually raised. The osmotic fragility of the patient's cells is characteristically decreased. The serum iron content is normal or increased. Bone-marrow examination shows erythroid hyperplasia, erythropoiesis being typically normoblastic. Megaloblastic change is known to occur in rare cases of intermediate severity during pregnancy, and is usually considered to be due to folic-acid deficiency.

Treatment.

There is no specific treatment. Iron should not be given, as there is a tendency to hæmosiderosis. Transfusion should be reserved for those patients in whom the anæmia produces serious symptoms, or when a sudden worsening of the condition occurs during infections or pregnancy. Splenectomy is reserved for those with excessive splenomegaly, or in whom there is severe hemolysis.

Clinical Record.

S., a female patient aged approximately 20 years, from the Milne Bay district was admitted to the General Hospital, Port Moresby, on July 18, 1960, for investigation of anæmia. The anæmia was known to have been present for at least two years, and to have become worse during a pregnancy, which had terminated in the birth of a male child 18 months previously. During this pregnancy she had been treated with iron by mouth, "Imferon" and folic acid, but her anæmia failed to respond and she was transfused on several occasions. After the birth of her child she returned to her village and received no further treatment. Apart from a history of tuberculous cervical glands, she had always been in good health, and was able to do her own housework and work in her garden without distress. Her diet was typical of the area in which she lived—namely, taro, sweet potatoes and yams, and fish about once a week.

The patient said that her parents had died of some unknown disease when she was a child. She had no siblings, and her father was also an only child. Her mother had three brothers, who are still alive.

On examination, she appeared reasonably well-nourished; she had pronounced bossing of her frontal bones and a "tall head". Slight mid-dorsal kyphosis, and slight out-

ward bowing of the humeri with hyperextensibility of the elbows were present. Otherwise the skeletal system appeared normal. The heart appeared normal apart from a systolic murmur of the ejection type, which was heard at all areas. There was no evidence of lung disease. The abdomen was prominent, and the liver was enlarged to four fingers' breadth below the right costal margin. The spleen was enlarged to the level of the umbilicus. There were a few moderately enlarged glands in the axillæ and inguinal regions.

Her male infant is now 18 months old, and his liver and spleen are both enlarged to two fingers' breadth below the costal margin. He has not yet been fully investigated; but there is some thickening of the frontal bones, and his hæmoglobin value is approximately 8 grammes per 100 ml.

A number of investigations were undertaken. The patient's hæmoglobin value ranged between 5·5 and 6·5 grammes per 100 ml. during her recent admission to hospital. The blood film showed microcytosis and hypochromia of the red cells, with considerable poikilocytosis. Numerous target cells and fragmented cells were observed, and nucleated red cells were present. The total number of white cells was within normal limits, and the distribution was not unusual.

On the day of her last admission to hospital, the blood film showed infection with *Plasmodium falciparum*, but these parasites were not found after treatment with chloroquine.

Dr. W. R. Pitney, of the Royal Perth Hospital, reported as follows on a bone-marrow smear:

> Fragments and fragment trails are hypercellular. There is intense erythroid hyperplasia. Erythropoiesis is normoblastic. Granulopoiesis appears depressed, megakaryocytes are present.

The result of the direct anti-human globulin (Coombs) test was negative, and the marrow smears contained hæmosiderin in large amounts. The diagnosis was established by the following report of hæmoglobin electrophoresis from Dr. Peter Brain:

> There is a major component with the mobility of hæmoglobin F, and alkali denaturation gives a concentration of 67% fœtal Hb. There is also a somewhat increased A_2 component. . . . The electrophoretic picture is consistent with thalassæmia major. The unusual feature is the high concentration of Hb F.

Examination of the stools revealed a few hookworm ova but no occult blood.

Dr. D. J. Bassett, of the General Hospital, Port Moresby, reported that there was pronounced thickening of the frontal bone, especially on the right side. The remainder of the vault had a granular appearance apparently due to widened diploë. Coarse trabeculation of the ends of both humeri was present, with widening of the medullary cavities and thinning of the cortices. Similar changes were present in the bones of the forearms, ribs, pelvis, femoræ, tibiæ and feet. These changes are illustrated in Figures I, II, III and IV.[1]

Discussion.

There are some unusual features in this case. The amount of fœtal hæmoglobin suggests thalassæmia major, as do also the bony changes, but it has often been observed that the anæmia is not directly related to either of these factors. It is not common for a person suffering from thalassæmia major to survive to the age of this patient, and successfully to complete pregnancy. However, Phaedon Fessas makes the following statement:

> As regards thalassæmia major the situation is somewhat different at least from the viewpoint of the clinician and the hæmatologist. It is really difficult to place under one heading cases of thalassæmia homozygotes who rarely reach puberty and might need one transfusion each month, with those reaching their 30th or 40th year of age with neither transfusions nor medical attention except under certain circumstances. For such cases the term "intermediate", as suggested by Sturgeon *et al.* (1955) might be useful and is more descriptive of the condition. Should it be known that such a patient is a homozygote, the term thalassæmia major of intermediate severity is probably indicated as being more adequate.

Another unusual feature is the absence of leucocytosis; but this may have been due to the presence of a heavy infection with *P. falciparum*, or perhaps to a splenic effect. There is a common hæmolytic anæmia with splenomegaly in Papua associated with leucopenia (unpublished observations). It is unfortunate that family studies cannot be carried out, but it is considered that the evidence outlined above is sufficient to classify this case as one of thalassæmia major of intermediate severity.

This is the first recorded example of thalassæmia in Papua, and there is no suggestion that the genetic factor responsible has been introduced by recent migrants from another country. It is therefore likely that further cases will be found in the Territory of Papua and New Guinea.

Acknowledgements.

My thanks are due to Dr. H. White, Acting Director of Department of Public Health, Territory of Papua and New Guinea, for permission to publish this case. Special thanks are due to Dr. W. Pitney, of the Royal Perth Hospital, for his reports on the peripheral blood and marrow films, to Dr. D. Curnow, Biochemist, Royal Perth Hospital, for his report on the alkali denaturation test, and to Dr. P. Brain of the Australian Red Cross (Western Australian Division). Thanks are also due to my colleagues at the General Hospital, Port Moresby.

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Addendum.

Since the foregoing case was described, two others have been diagnosed, one from Kenema and one from Oro Bay.

[1] For Figures I-IV see art-paper supplement.

Reviews.

Rose and Carless: Manual of Surgery. Consulting editor, Sir Cecil Wakeley, Bt., K.B.E., C.B.; editors, Michael Harmer and Selwyn Taylor, assisted by fifteen contributors; nineteenth edition; 1960. London: Baillière, Tindall and Cox. 9½" × 6", pp. 1408 with many illustrations. Price: 84s. (English).

IT is always pleasant to greet an old friend again, especially one who, when last seen, seemed to be showing the signs of age, and who now, on renewal of acquaintance, is discovered not only to have recaptured his lost youth, but to have retained the wisdom of his years. The editors and various authors of the nineteenth edition of Rose and Carless' "Manual of Surgery" are to be congratulated on achieving this seemingly impossible metamorphosis, and thereby giving a new and sparkling lease of life to a work which has been held in high regard for more than 60 years.

The original edition, first published in May, 1898, must surely have been one of the first "encyclopædic" textbooks of surgery, and its value has been such that new editions were regularly produced every few years, with minor breaks during and after the World Wars. William Rose and Albert Carless were surgeons on the staff of King's

College Hospital, and brief but graceful biographies of the two original authors are properly added to this edition. Their dedication of the volume to Lord Lister, who achieved so much in their hospital, is retained. The King's College Hospital tradition has been maintained in the present edition.

Those who knew an older edition will recognize many of the splendid photographs, line drawings and coloured illustrations, which were models of simplicity and clarity; but some 370 new ones have been added, and these have kept up these standards admirably. The text has been extensively rewritten, some chapters have been redesigned, and others—notably sections on malignant disease, endocrine glands and pædiatric surgery—have been added. The scope of this work is very wide, and topics which would have seemed bizarre indeed to the original authors are included, such as open heart surgery, the artificial kidney and antibiotics as up-to-date as novobiocin, vancomycin and ristocetin. The material is, after the earlier manner, divided into sections, placed in orderly and logical sequence, so that, in spite of its overall size, it retains a useful digestibility for the undergraduate student, yet, because of its completeness, it could well be of value to the graduate seeking a higher qualification. The production of this volume is a credit to the publishers, and the present authors, Michael Harmer and Selwyn Taylor, have done a service not only to the undergraduates and graduates of the future, but also to those mature enough to possess a sense of history and a wholesome respect for the great British tradition of surgery and surgical teaching.

Demonstration of Physical Signs in Clinical Surgery. By Hamilton Bailey, F.R.C.S., F.A.C.S., F.R.S.E.; thirteenth edition; 1960. Bristol: John Wright and Sons Limited. 8¾" × 5½", pp. 942, with 1142 illustrations. Price: 75s.

ANY new edition of Hamilton Bailey's well-known book would naturally excite renewed interest and further admiration, and the latest (thirteenth) edition does just that. Sir Henry Wade's dictum, "The wards are the greatest of all research laboratories", continually needs reemphasizing nowadays, and is truly implemented by this more comprehensive and larger volume, which is extraordinarily popular in many countries.

The lavish and beautiful illustrations are well placed and educative in themselves, without even the reading of the text. Some old illustrations have been retained and reappear like old friends, while many others have been replaced or added. Indeed, the illustrations are part and parcel of the book, and suitable acknowedgement is made to their various sources from many parts of the globe. If any improvement is to be found in future editions, it may well be with even better and better illustrations.

Redrafting of the text is evident in several sections, and only minor unimportant items could be raised. For instance, on page 244 one could add irradiation to the thymus as a precursor of malignant disease of the thyroid. Generally one can find little fault in the descriptive writings of this master of clinical signs.

This book has grown considerably in size and price, but nevertheless it will always be essential and profitable to own.

A History of Psychiatry. By Jerome M. Schneck, A.B., M.D.; 1960. Springfield, Illinois: Charles C. Thomas; Oxford: Blackwell Scientific Publications Ltd. 9" × 5¾", pp. 208. Price: 44s. (English).

DR. JEROME M. SCHNECK opens this book with a discussion of primitive societies and archaic medicine, in which he follows James Frazer's theories of similar and contagious magic in explanation of primitive therapeutic rituals and practices. Reference is made to Professor Elkin's "Men of High Degree". Observation of the pulse rate in response to a list of names as a complex-indicator was described by Erisistratus (310-250 B.C.) and continued to be mentioned in medical works for several centuries (Celsus, Avicenna).

In the chapter on the Renaissance, Johannes Wierus (1515-1588) receives special mention for his interest in mental disorders, but there is no reference to Jean Fernel (1497-1588), whose writings on the age-long problem of mind-body relationships were widely read (Sherrington, "Man and his Nature", 1940). The seventeenth century, the period of René Descartes, William Harvey, Thomas Sydenham and Thomas Browne, saw the dawn of more enlightened attitudes despite lingering beliefs in witchcraft supported by prominent physicians.

By the eighteenth century, psychiatry was becoming somewhat of a specialty, though treatment remained mostly in the hands of general physicians. Franz Anton Mesmer (1734-1815) propounded his theory of animal magnetism (1779), and John Wesley claimed that "hundreds, if not thousands had benefited from the application of an electrical apparatus". Electrical machines were used at St. Bartholomew's Hospital and St. Thomas' Hospital. At the end of the century Pinel (1745-1826) discarded phlebotomy and reduced the use of mechanical restraint in the Salpétrière, and introduced his system of "moral" therapy, which included occupation and recreation.

Emil Kraepelin (1856-1926) consolidated previous and contemporary descriptions and classifications, and initiated a biological and ecological approach. His contemporary, Freud, and the psycho-analytical deviationists and modifiers, Jung, Adler, Wilhelm Steckel, Otto Rank, Karen Horney and Harry Stack Sullivan, receive mention in some detail.

While the present position is one of uncertainty, if not of complete ignorance, as to the essential dynamics of physical and more particularly psychological treatment of mental disorders, Dr. Schneck hopes that the not distant future will see integration of viewpoints and techniques with a less empirical approach.

The work is essentially factual and, though comprehensive, remains readable. It is commended to all—and who should not be?—who are interested in the history of their specialty.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"The Organization of Cells and Other Organisms", by Laurence Picken; 1960. Oxford: The Clarendon Press. 9¼" × 6", pp. 668, with many illustrations. Price 121s.

"A Textbook of Clinical Pathology", edited by Seward E. Miller, M.D.; sixth edition; 1960. Baltimore: The Williams & Wilkins Company. 10" × 6¾", pp. 916, with illustrations. Price: £8 5s. 0d.

"Modern Trends in Occupational Health", edited by R. S. F. Schilling, M.D., M.R.C.P., D.P.H., D.I.H.; 1960. London: Butterworth & Co. (Publishers) Ltd. 9¼" × 6¼", pp. 338, with illustrations. Price: 92s. 6d.

"Nature of Rheumatic Heart Disease: With Special Reference to Myocardial Disease and Heart Failure", by George E. Murphy, M.D.; 1960. Baltimore: The Williams & Wilkins Co. 10" × 6¾", pp. 99, with 162 photomicrographic illustrations in colour. Price: 38s. 6d.

"The Care of Invalid and Crippled Children", edited by A. White Franklin, M.B., F.R.C.P.; 1960. London: Oxford University Press. 7¼" × 4¾", pp. 174. Price: 14s. 3d.

"Antisera, Toxoids, Vaccines and Tuberculins in Prophylaxis and Treatment", by H. J. Parish, M.D., F.R.C.P.E., D.P.H., and D. A. Cannon, O.B.E., M.B., B.Sc., D.T.M. & H.; fifth edition; 1961. Edinburgh and London: E. & S. Livingstone Ltd. 8¾" × 5¾", pp. 296, with illustrations. Price: 37s. 6d. net (English).

"Anatomy and Physiology for Radiographers", by J. E. Blewett, M.D., D.M.R., F.F.R., and A. M. Rackow, B.Sc., M.B., D.M.R.E.; 1960. London: Butterworth and Co. (Publishers) Ltd. 8¾" × 5¼", pp. 372, with illustrations. Price: 52s. 6d.

"Principles of General Neurophysiology Relating to Anæsthesia and Surgery", by Barry D. Wyke, M.B., B.S. (Sydney); reprinted from "General Anæsthesia", Volume I, edited by Frankis T. Evans and Cecil Gray; 1960. London: Butterworth & Co. (Publishers) Ltd. 8¼" × 6¼", pp. 146, with illustrations. Price: 30s.

"Ciba Foundation Symposium on Hæmopoiesis: Cell Production and its Regulation", edited by G. E. W. Wolstenholme, O.B.E., M.A., M.B., M.R.C.P., and Maeve O'Connor, B.A.; 1960. London: J. & A. Churchill Ltd. 8" × 5¼", pp. 502, with illustrations. Price: 60s. net (English).

"Surgical Treatment of Unequal Extremities", by Charles Weer Goff, M.D.; 1960. Springfield, Illinois: Charles C. Thomas, and Oxford: Blackwell Scientific Publications Ltd. 11" × 8½", pp. 194, with illustrations. Price: 88s. (English).

"Clinical Applications of Cardiopulmonary Physiology", by M. Henry Williams, Jr., M.D.; 1960. New York: Paul B. Hoeber, Inc. 9¼" × 6", pp. 246. Price: $7.50.

The Medical Journal of Australia

SATURDAY, JANUARY 28, 1961.

THE NURSE IN SOCIAL MEDICINE.

THE development of nursing in its modern form has been proceeding for little more than a century. Long before that, under the ægis of various religious orders, nuns had undertaken the care of the sick and aged, at their homes and in infirmaries; and in those early days the nurse's function was a wide one, embracing much of what now is classed as social work. In the new era of nursing, beginning in 1854, when Florence Nightingale and her co-workers instituted the training course at St. Thomas's Hospital in London, the duties involved in the care of the sick were mainly performed in hospitals. At the same time it should be remembered that the Fliedners in Germany, whose work inspired Miss Nightingale in her unflagging efforts, gave training to their deaconesses in nursing and in social work; the patients were visited in their homes, advised and cared for. It is interesting therefore to note that this important aspect of nursing, its integration with the home-life of the people, has been given much attention again in recent years. Besides district nursing, which involves the nursing care of sick people in their homes, and which has developed in a number of worthwhile forms in Australia, there has come in other parts of the world health visiting—a nursing *cum* social work function. In Britain it appears that the National Health Service has stimulated developments in that way; a new edition of the "Textbook for Health Visitors" by L. Roberts and C. H. Shaw[1] provides a clear indication of the scope and nature of the work there today.

As is well known, the hospital organization in the National Health Service is under the immediate control of the 14 regional boards, the health services are under local health authorities, and the general medical services are under executive councils. This tripartite scheme needs careful coordination in its workings to ensure efficiency, and the trained health visitors are able to assist in this integration. The *National Health Service Act* provides that local health authorities shall employ health visitors "for the purpose of giving advice as to the care of young children, persons suffering from illness and expectant or nursing mothers, and as to measures necessary to prevent the spread of infection". The provision of health education and social advice makes up the health visitor's principal functions. She is responsible to the Medical Officer of Health, and through him practitioners and hospitals may get her help.

What is termed the "integrated course" in the training of health visitors involves: (i) An academic year at Southampton University (or some other approved institution), where the studies include general aspects of nursing, psychology, anatomy and physiology, and social science. (ii) The three years' training at St. Thomas's Hospital, and the final examination in nursing. (iii) An obstetric course at St. Thomas's Hospital (eight months). (iv) A final period (two terms) at the University; social psychology, case-work, mental disorders and epidemiology are some of the studies. (v) The Royal Society of Health examination for health visitors, at the end of the fifth year of the comprehensive course. It is interesting that St. Thomas's Hospital, so closely linked with the Nightingale tradition, is the centre-piece of this present-day development in nursing. Just a century ago, in 1860, a training institute for nurses—the first in Britain—was established at St. Thomas's.

The doctor in his daily work is coming to depend more and more on the auxiliaries, which are steadily increasing in number and variety. The health of people in relation to their social environment is engaging the attention of many groups and professions: physicians, psychiatrists, local health and hospital authorities, hospital almoners, and social workers, as well as a great variety of voluntary and charitable bodies. In such circumstances it is vitally important to avoid confusion in the management of people's ills and in the advice given. Nothing is more likely to shatter the patient's confidence in his advisers than any inconsistency in the pieces of information they may give him. It would appear that the smooth, harmonious and effective working of Britain's Health Services depends in no small measure on the cooperation of the several groups. The health visitor, well trained as a nurse and social worker, takes an important part in the scheme, and the success achieved indicates that the professional training of a nurse is a good basis for the best type of social worker. In Australia, the profession and training of health visitors has yet to develop—the beginnings have appeared, for the Colleges of Nursing are alert in the matter in their post-graduate training courses. In Britain the programme is fast under way, and in this regard the general practitioner, assisted by the medical officer of health and the health visitor, has the opportunity to build a real National Health Service, with the emphasis on Health, and a world model for preventive medicine.

The modern nurse in her specialized setting as a health visitor has assumed the functions of her early prototype—the nun-nurse-social worker of the early Christian era. There is the difference that the health visitor of today has to be acquainted with a large amount of fundamental and applied knowledge of nursing and social science, has to undergo arduous training in those fields, and has to be examined and registered for her duties. Hers is a medico-social vocation worth careful consideration, and one likely to appeal to a thoughtful and intelligent nurse. What place, if any, it will have in Australia's future health services has yet to be determined. One side comment,

[1] "Textbook for Health Visitors", by Llywelyn Roberts, M.D., M.R.C.P., D.P.H., Beryl D. Corner, M.D., F.R.C.P., and C. H. Shaw, M.D., M.R.C.S., D.P.H.; second edition; 1960. London: Baillière, Tindall and Cox. 7¾" × 5", pp. 516, with illustrations. Price: 32s. 6d. (English).

however, is clear: with modern developments in nursing, the status of the profession continues to rise. Never has Osler's dictum been more true: "There is no higher mission in life than nursing God's poor."

Current Comment.

RHEUMATIC HEART DISEASE.

RESEARCH into rheumatic heart disease has progressively yielded a series of important facts and a good deal that is still speculative. It has been shown that many tissues, especially vascular structures, throughout the body are injured in attacks of rheumatic fever, and that the most serious damage occurs in the heart, to the myocardium and to its valves. It is generally considered now to have been conclusively shown that infections of body tissues with type A hæmolytic streptococci play a causative and key role in the pathogenesis of this disease, but only a small proportion of human beings infected with type A streptococci develop rheumatic heart disease. It is also widely held that the rheumatic lesions in the myocardium, including the so-called Aschoff bodies, are non-myogenic lesions of the connective tissue and do not involve the heart muscle fibres. However, G. E. Murphy,[1] in a long and very detailed paper, subsequently reprinted as a monograph,[2] has set out to demonstrate that this last-mentioned interpretation is not correct, and that it is the heart muscle and plain muscle fibres which are affected. He was able to produce typical cardiac changes in a small proportion of rabbits with multiple focal infections due to type A hæmolytic streptococci, and these gave material for study at various stages of the cardiac changes. In addition, he made a detailed microscopic study of the hearts of over 100 patients who had died with active rheumatic heart disease and of the left atrial appendages removed from 150 other patients at the time of mitral commissurotomy. The histopathological findings are presented in considerable detail with 162 beautiful reproductions of coloured sections of cardiac tissue illustrating the points made in the text. A study of the text and the slides makes clear the author's claims that the changes in the myocardium, both in man and in rabbits, are really in the muscle cells and not in the fibrous tissue.

Murphy states that in fatal cases of acute rheumatic heart disease the ventricular chambers, particularly the left, are generally dilated. This may be seen when neither valvular deformity nor pericardial adhesions are present and is associated with dilatation of the atrio-ventricular valve rings. He believes that the muscle lesions in the myocardium in rheumatic hearts weaken the muscles and so allow stretching of the myocardium and of the valve rings. In relation to this, detailed accounts from the literature are given of changes in the heart in rheumatic disease described by previous authors.

Murphy claims to have demonstrated that the characteristic constituents of myocardial Aschoff bodies are of two types: (i) mononucleated, multinucleated or non-nucleated fragments of damaged muscle cells, and (ii) multinucleated syncytial masses of myogenic origin that proliferate from inside the sarcolemma into tracks of disintegrating muscle cells and appear in the beginning to represent attempts at regeneration of heart muscle cells. He details the probable course of the changes from necrosis of muscle cells to the so-called Aschoff bodies. Short of these changes there is impairment of muscle cells with some recovery. Changes of a similar nature are also described in smooth muscle cells in the heart. In most fatal cases of active rheumatic heart disease with little or no valvular deformity, it appears that Aschoff bodies, especially the florid ones, do not occur in great enough number to account, in themselves, for myocardial failure. In most of these cases non-proliferative changes in the muscle fibres are prominent.

Murphy quotes Sir Thomas Lewis: "Failure [in cases of rheumatic heart disease] is due in part to the unusual burdens of work that the heart has to bear . . . but the chief factor must be inherent in the muscle itself, for failure can occur without the increased burden. And yet muscle that has failed cannot at present be recognized histologically or biochemically." Summing up the results of his own observations he comments:

> Evidence here presented and illustrated demonstrates the origin of rheumatic myocardial lesions, including the so-called Aschoff bodies, from heart muscle cells themselves, and the origin of other rheumatic cardiac lesions from smooth muscle cells. If active rheumatic disease of heart muscle cells can cause failure of children's hearts without the burden of valvular deformity, then it is likely that active rheumatic disease of heart muscle cells can cause failure of adult hearts, especially those burdened with valvular deformity and with myocardium damaged by previous attacks. Derived from experiment and histopathologic study, findings here presented and viewed in relation to clinical observations provide strong evidence of the very important causative relation of rheumatic disease of heart muscle cells to altered function and failure of the heart in acute and chronic rheumatic heart disease in children and adults.

This is an important development in thought on the subject, based on painstaking investigation. It must command a good deal of attention.

[1] *Medicine*, 1960, 39: 289 (September).

[2] "Nature of Rheumatic Heart Disease: With Special Reference to Myocardial Disease and Heart Failure", by George E. Murphy, M.D.; 1960. Baltimore: The Williams & Wilkins Co. 10" × 6¾", pp. 99, with 162 photomicrographic illustrations in colour. Price: 38s. 6d.

THE ODOUR OF INSANITY.

THERE must be a considerable body of fragments of clinical lore which never find their way into text books, or if they do, receive only cursory mention, because they are largely subjective impressions and it is not easy to test their validity. Every now and then some such fragment is taken out and dusted, and some ingenious investigator attempts to put it to a test the results of which can be expressed in terms of statistical probability. Kathleen Smith and J. O. Sines[1] have recently done this for the belief that "there is an odour peculiar to the insane", a statement attributed by them to H. Laehr in 1878, and since repeated in various guises. They state that this unusual odour seems to be especially intense in the room where insulin therapy is given, and appears to come from the skin of the patients, particularly those catatonic patients with greasiness of the skin. As smell is the most subjective of all human senses, and as in many human beings this sense is poorly developed, it was necessary to appeal to some independent arbiter, and a conditioning experiment was designed with the rat as the test animal. Long-stay patients were screened alphabetically till 14 white male schizophrenics were found who fulfilled the following criteria: possession of an intense characteristic odour, which is heavy, unpleasant and slightly pungent; a duration of illness in excess of 20 years, with an onset after the age of 18 years but before 30 years; no serological evidence of syphilis; continuous residence in a back ward of a State mental hospital for the previous 10 years. These were compared with a control group of 14 white male non-schizophrenic patients who suffered from various organic brain syndromes and lived in the same back wards for similar periods, eating the same diet and participating in the same activities. Samples of sweat were obtained from each patient, and it was found that the odoriferous substance could be extracted and concentrated with ether. Cotton wool soaked in this extract was used in the animal experiments, in which water-deprived rats were taught to recognize the odour of the sweat from schizophrenic patients as a guide to the box containing water. In the test trials the

[1] *A.M.A. Arch. gen. Psychiat.*, 1960, 2: 184 (February).

proportion of correct choices was 0·70, a result statistically significant at the 0·0001 level of confidence. The extracts were also submitted to a human odour-testing panel, consisting of three chemists whose job entailed detecting odorous impurities in flavourings and other high-grade chemical products. This panel achieved a proportion of correct results which was significant at the 0·005 level of confidence.

These experiments appear to demonstrate that the odour which is considered by some clinicians to be associated with schizophrenia can be discriminated both by human odour testers and by trained laboratory animals when sweat from selected schizophrenic patients is compared with that from non-schizophrenic patients considered to lack this odour. Smith and Sines admit that the distribution of this allegedly characteristic odour has not yet been adequately investigated. It may be present in many non-schizophrenic persons, and is apparently not universal among diagnosed schizophrenics. It has been suggested that it becomes weakened or undetectable during a remission of schizophrenia and reappears during an exacerbation. It has been noted in schizophrenics of both sexes.

The suggestion that schizophrenia is associated with some specific metabolic disturbance has led to many as yet unrewarding investigations, and Smith and Sines suggest that the identification of the substance responsible for this characteristic odour may give a useful lead in this direction. Attempts to identify this substance have so far proved unsuccessful; it is not unlikely that it is present only in very minute quantities. The question arises whether the odour is due to a metabolic product or whether it is due to bacterial action. Scrubbing patients with surgical soap or with hexachlorophene, followed by thorough rinsing, failed to inhibit the odour, suggesting that it is due to a metabolic product from apocrine sweat or from sebaceous gland secretion. Clearly much remains to be done before the subject can be considered to have been at all adequately investigated, but it appears to hold interesting possibilities.

PERMISSIBLE DOSE FOR INTERNAL RADIATION.

THE task of Committee II of the International Commission on Radiological Protection[1] is to recommend values for maximum permissible body burdens of radionuclides, q, and maximum permissible concentrations of these nuclides in air, (MPC)a, and in water (or food), (MPC)w. The importance of these values lies in the fact that once a person has obtained an internal body burden of a radionuclide, little can be done to hasten its removal from the body. The radium dial painters are a constant reminder. The fact that these substances are carcinogenic and mutagenic provides cogent reasons for collating all biological and physical data and setting limits for occupational exposure and for exposure of the population at large. In this revision of the 1958 report, the MPC values have been brought up to date from the results of research to the end of 1957. As such, they represent the best available values, although it is realized that their basis is sometimes incomplete and uncertain.

Just as there are theoretically two ways to control X-ray exposure in medicine, so there are two possibilities for controlling the exposure of personnel in a plant to radionuclides. Rather than have the uncertainty of keeping individual exposure records, it is far safer to keep the level of radiation exposure in a department below the recommendations for external exposure. Similarly, the safest and simplest procedure in the case of internal exposure is to keep the level of contamination of the air, water or food in the controlled area at or below the level indicated by the MPC values. These values are given for about 240 radionuclides for exposure periods based on the 40-hour week and the 168-hour week. The values for inhalation and ingestion in the critical organ are given in bold face type. If there is also occupational external radiation exposure, then the MPC values must be reduced by the factor (D–E)/D, where D rem is the dose permitted to an organ by the basic rules and E rem is the external radiation exposure over a similar time period. It has been recommended that medical or dental exposure be excluded from the calculation of the maximum permissible dose for those occupationally exposed.

The maximum permissible exposure values have been calculated from the basic rules of the International Commission on Radiological Protection Report:[2]

(47) The maximum permissible total dose accumulated in the gonads, the blood-forming organs and lenses of the eyes at any age over 18 years, shall be governed by the relation D = 5 (N-18) where D is tissue dose in rems and N is age in years.

(48) For a person who is occupationally exposed at a constant rate from age 18 years, the formula implies a maximum weekly dose of 0·1 rem.

However, for bone-seeking radionuclides, the estimate is based on a comparison with ^{226}Ra, i.e., the amount ($\mu c.$) deposited in the bone that will deliver the same effective RBE dose as delivered by 0·1 $\mu c.$ of ^{226}Ra and its daughter products. This amounts to a dose rate of 0·56 rem per week derived from a dose rate of 0·06 rad per week and an RBE of 10. For other critical organs the International Commission on Radiological Protection recommendations apply, i.e., 0·6 rem per week to the skin and thyroid, and 0·3 rem per week to all other soft tissues, except where toxicity of the radionuclide sets the limit.

The occupational levels (168-hour week) permit 5 rems per year, but when considering exposure of the population at large, Committee II has suggested that the average permissible level for consideration of the somatic effects of radiation be one-thirtieth of the occupational level. When considering the genetic effects of radiation to the population at large, the 1958 International Commission on Radiological Protection recommendations gave for guidance a total dose of 1·5 rems over the genetically significant thirty-year period for internal radiation. Since the continuous occupational levels (168-hour week) allow 150 rems in 30 years to the gonads, the MPC value must be multiplied by a factor of 0·01 when calculations are being made for the population at large. In the absence of an MPC value based on the gonads, the whole body value can be used, but it should be remembered that it is doubtful if many of the nuclides contribute much to the genetic load.

[1] "Report of Committee II on Permissible Dose for Internal Radiation (1959); Recommendations of the International Commission on Radiological Protection", ICRP Publication 2; 1959. London, New York, Paris, Los Angeles: Pergamon Press. 10" x 7", pp. 266. Price: not stated.

[2] Recommendation of the International Commission on Radiological Protection, 9th September, 1958", Pergamon Press, London.

NUFFIELD ASSOCIATE PROFESSORSHIP IN ANÆSTHESIA.

THE Nuffield Foundation has announced that a grant of £25,000 has been made to the University of Sydney to establish a Nuffield Associate Professorship in Anæsthesia. This grant has been arranged by Professor John Loewenthal, Professor of Surgery in the University of Sydney, and it is planned that the new associate professor will take up his duties in close association with the department of surgery in that University. This appointment should help with the problems of teaching of and research in anæsthetics — problems which are becoming progressively more difficult because of the increasing complexity of modern anæsthetics and because of the hazards involved with some of the newer methods necessary for complicated modern surgery. The establishment of this associate professorship, the first of its kind in Australia, marks a real advance and warrants congratulations to the Nuffield Foundation, to the University of Sydney and to Professor Loewenthal. We wonder, however, if it might not be better called a professorship of anæsthetics.

Abstracts from Medical Literature.

HYGIENE.

Incidence of Coagulase-Positive Staphylococci in a Normal Unconfined Population.

S. MILLIAN *et alii* (*Amer. J. publ. Hlth*, June, 1960) report on a study undertaken to determine the incidence of coagulase-positive staphylococci in an unconfined normal population, to serve as a comparison with carrier-rates found in hospitals, and to discover any other significant facts regarding carriers. Nasal swabs from 577 apparently healthy applicants for food-handling positions were examined. Of 147 white females, 37%, and of 271 white males, 38% were found to be carriers. Of 87 Negro females, 20%, and of 72 Negro males, 10% carried coagulase-positive staphylococci. Statistical evaluation of the data indicated that nasal carriage of *Staphylococcus aureus* was associated with race. No significant relationship could be shown between carrier rate and sex, age or season.

Response of Infants to a Multiple Vaccine.

G. C. BROWN AND P. L. KENDRICK (*Amer. J. publ. Hlth*, October, 1960) discuss the serological response of infants to a multiple vaccine for simultaneous immunization against diphtheria, pertussis, tetanus and poliomyelitis in relation to the presence of specific maternal antibody. They investigated immunological response in the presence of specific antibody—actively produced or passively acquired by the infant as maternal antibody—in 48 infants from two to four months of age, who were injected three times at intervals of one month with 0·5 ml. of a multiple vaccine against diphtheria, tetanus, pertussis and poliomyelitis. Thirty-one of the children received an additional or booster dose from 6 to 12 months later. Serological tests on pre-vaccination blood specimens revealed that very few of the infants had detectable antibodies to diphtheria, tetanus or pertussis, but the majority of them had poliomyelitis antibodies at this time. The response of the majority of the infants to the poliomyelitis components of the vaccine was definitely poorer than to the diphtheria, tetanus and pertussis components. The lower serological response to the poliomyelitis antigens was considered to be clearly associated with the presence of maternally acquired passive antibodies in the infant's serum at the time of vaccination. The few children who had pre-vaccination antibodies to diphtheria, tetanus and pertussis also had poorer response than did those who had no such antibodies before vaccination. The suppressive effect of maternal antibodies affected not only the primary, but also the booster response to the several antigenic components; tetanus antibody production seemed to be least influenced. The authors consider that these findings suggest that consideration should be given to delaying poliomyelitis vaccination until maternal antibodies have disappeared or have been reduced to a low level.

Airport Sanitation.

L. F. WESTBROOK AND E. REED (*Publ. Hlth Rep.* (*Wash.*), September, 1960) describes how the health of people using a new American international airport is maintained. Sanitation services were considered early in the planning of the airport. The building of such installations as aircraft catering kitchens and facilities for storing, preparing and serving food for employees and patrons was supervised by an officer of the health authority concerned. The same officer was placed on full-time duty at the airport on its completion. All garbage is stored in metal fly-proof, leak-proof, roll-away containers and removed daily by private contract. Other wastes, including human excreta collected from aircraft, are treated in triturators, and all containers used for storage and transport of this material are cleaned and treated chemically. Hot and cold water from tanks filled from, but disconnected from, the city water supply is used for cleaning. Potable water is supplied to aircraft from taps which are used for this purpose only. In addition to supervision of waste disposal, potable water supply, catered airline meals, and meals for airport employees, the officer is concerned with health cards for food handlers, rodent and insect control, animal quarantine, inspection of aircraft galleys, restaurant dish-washing and glass-cleaning equipment, frozen food storage and intermittent emergencies. Examples are then given by the authors of actual tasks done by the officer stationed at the airport. A list of future requirements is then given. These included the provision of means of barring stray dogs from the airport and all dogs, except "seeing eye" dogs, from eating places, and the provision of a method for keeping out of air conditioning systems oil mists released from jet engines.

Microbiological Standards for Foods.

A REPORT (*Publ. Hlth Rep.* (*Wash.*), September, 1960) gives the conclusions of a conference called by the Division of Medical Sciences of the National Academy of Sciences—National Research Council to discuss microbiological standards for foods. The conference agreed that microbiological standards are desirable and in some cases necessary. Classification of food products for application of standards was found to depend on a number of factors, but very few foods were considered to be completely free from hazards of contamination in all circumstances. The coliform count, the standard plate count and *Escherichia coli* count were all considered to be appropriate tests under different circumstances. It was considered that there was no single standard test suitable for all foods. The conference agreed that present epidemiological knowledge was insufficient to base precise limits for organism counts in various tests. It was suggested that limits be based on numbers and types of organisms present under good practice. The conference also agreed that microbiological standards were not sufficient alone to protect consumers from infected, poisoned or spoiled food, and that further advances in the knowledge and practice of sanitation by professionals and technicians, commercial interests and consumers were required. Opinions expressed by members of the conference are then recorded.

Toxicity of Diborane in High Concentrations.

A. R. STUMPE (*A.M.A. Arch. industr. Hlth*, June, 1960) has studied the effect of high concentrations of diborane on hamsters. Toxic signs and pathological evidence of severe pulmonary damage were observed. As the concentration of diborane was increased from 50 p.p.m. (58 mg. per cubic metre) to 600 p.p.m. (696 mg. per cubic metre), the mean survival time for exposed hamsters decreased. Also noted was a progressive narrowing of the time interval for all exposed animals to die. However, concentrations in excess of 600 p.p.m. elicited no further reduction in the minimum, maximum or mean exposure times for death. Understanding of the mechanism of action of diborane is not complete. In view of diborane's extreme toxicity it becomes imperative that future aircraft and rockets utilizing the boranes as high-energy fuels be designed to provide the utmost protection against accidental cabin air contamination. Diborane can exist in the atmosphere above the maximum allowable concentration of 0·1 p.p.m. without its characteristic odour of "rotten eggs" being perceptible. Treatment of the accidentally exposed person is supportive and symptomatic.

Significance of Fæcal Streptococci.

C. H. BARTLEY AND L. W. SLANETZ (*Amer. J. publ. Hlth*, October, 1960) have investigated the types of streptococci found in samples of water, sewage and human and animal fæces and discuss their sanitary significance. Over 5000 strains were isolated. For comparative purposes coliforms were also isolated and identified. The membrane filter technique was used. Details of methods used and results obtained are given. In conclusion the authors consider that the results indicate that membrane filter tests for fæcal streptococci are more practical, efficient and accurate than coliform tests for evaluating the sanitary quality of almost all types of water, and conclude that these tests deserve serious consideration by everyone interested in improving bacteriological procedures for water analysis.

Lung Cancer Mortality.

J. E. DUNN *et alii* (*Amer. J. publ. Hlth*, October, 1960) report the results of a prospective study in which populations of Californian workers engaged in some suspect occupations were assembled, and their lung cancer experience observed during succeeding years. The study began in 1954 and this report is based on death experience to 1958. It was found that most of the occupations studied have a larger proportion of cigarette smokers and a heavier cigarette consumption than is true for the control population. The latter appears to be quite representative of Californian males generally

in respect to cigarette smoking. Relative risks for each occupation as compared to the control population are computed, the smoking distribution of the controls being considered as representing unit relative risk. Correcting the observed lung cancer deaths for the apparent deficit in the study conditions and the expected lung cancer deaths for smoking practice leaves at least two occupations with tentative excesses of lung cancer risk. These are cooks and painters. The order of magnitude of over-all increased lung cancer risk to be expected in these populations now appears to be in the one and a half-fold to two-fold range. This would represent an increased risk from the occupational exposure in the range of five-fold to nine-fold for non-smokers, if the occupational factors were acting independently from the smoking factor.

PHYSIOLOGY.

Drowning Treated with Intermittent Positive Pressure Breathing.

J. REDDING *et alii* (*J. appl. Physiol.*, September, 1960) report that a standardized dog experiment was designed to simulate human victims of submersion who seem to develop first laryngospasm, followed by flooding of the lungs. The tracheal tube of lightly anæsthetized dogs was clamped until the onset of apnœa. The lungs were then flooded for 30 seconds with fresh water or sea water, or apnœa was permitted to continue for a comparable period without flooding. Resuscitation was attempted with intermittent positive pressure breathing (IPPB), utilizing room air. All control dogs (obstructive asphyxia, without flooding) survived. Fresh-water drowning caused mild arterial hypotension, severe rise in venous pressure and bradycardia, followed by sudden ventricular fibrillation in 1 to 4 minutes in spite of IPPB. Sea-water drowning caused severe arterial hypotension, slight rise in venous pressure and bradycardia. IPPB led to partial reoxygenation and partial restoration of circulation. When IPPB was discontinued all dogs started breathing spontaneously, but within a few minutes developed asystole with pulmonary œdema.

Olfactory Acuity and Nasal Membrane Function.

R. A. SCHNEIDER AND S. WOLF (*J. appl. Physiol.*, September, 1960) state that the relationship between olfactory perception threshold and accompanying degrees of nasal obstruction, swelling, colour and wetness was studied in eight subjects over a prolonged period. Olfactory acuity was impaired in two situations: (*a*) in the presence of high degrees of nasal obstruction so that relatively little of the odorant-containing air could be brought into the nose; (*b*) in the absence of obstruction when the mucosa was relatively pale, dry and shrunken. During intermediate degrees of nasal obstruction when substantial amounts of air could be drawn into the nose, relatively high degrees of swelling, redness and wetness favoured olfactory acuity. Thus smelling was best performed in the presence of a red, swollen, wet mucosa as long as swelling and secretions were not of such a degree as substantially to block air passage. The evidence suggests that contact of odorant with nerve endings is facilitated by the greater warmth and humidifying effect of nasal engorgement during hyperfunction of the "air-conditioning" apparatus of the nose.

Experimental Enlargement of Submandibular Salivary Gland.

H. WELLS AND P. L. MUNSON (*Amer. J. Physiol.*, July, 1960) report that an increase of 12% in fresh and dry weight of the submandibular salivary glands was observed 24 hours after a single amputation of the lower incisor teeth. This effect was increased by repeated amputations, and was further intensified by increasing the frequency of amputations and by lengthening the period of amputations. After cessation of a series of amputations, the weight of the hypertrophied salivary glands decreased gradually to approach the control level. Repeated amputation of only one lower incisor tooth was much less effective than amputation of both, and the effect was largely but not entirely restricted to the ipsilateral glands. Ulceration of the adjacent mucosa without amputation of the incisors had no detectable effect on the salivary glands. After amputation of the tips of the incisor teeth without exposure of the pulp or after half-amputations with minimum exposure, the salivary glands increased in weight significantly but much less than after amputation at the gingival margin. It is concluded that the data support the reflex neurological explanation of the phenomenon previously offered by the authors.

Control of Respiratory Frequency.

J. MEAD (*J. appl. Physiol.*, May, 1960) states that previous work has shown that for a given level of alveolar ventilation there is a particular respiratory frequency which is least costly in terms of respiratory work. There is also a particular frequency, usually a different one, which is least costly in terms of average force of the respiratory muscles. Evidence is presented that in the resting guinea-pig and in man at rest and during exercise natural breathing takes place at frequencies approximating the second optimum. From additional observations on the effects of changing the mechanical characteristics of the respiratory system on respiratory frequency it is concluded that the principal site of the sensory end of the control mechanism is in the lungs.

Carbon Dioxide Buffering in Man.

L. B. BERMAN *et alii* (*J. appl. Physiol.*, May, 1960) report that the administration of tris(hydroxymethyl)aminomethane (THAM) to six normal adults was followed by a series of changes in ventilation, arterial blood and urine. Alveolar ventilation and oxygen saturation fell significantly, as did alveolar carbon dioxide excretion and tidal volume. Alveolar and blood carbon dioxide tension rose slightly. The blood bicarbonate level rose, while other electrolyte levels were essentially unchanged. Urinary pH and electrolyte excretion increased strikingly without any change in endogenous creatinine clearances. No toxic effects were observed. The findings suggest that THAM cannot presently be recommended for clinical use in the treatment of respiratory acidosis, unless some means of stimulating respiration are also provided.

Autoregulation of Intestinal Blood Flow.

P. C. JOHNSON (*Amer. J. Physiol.*, August, 1960) reports that previous experiments have shown that the arterial vessels of the intestine are responsive to changes in portal venous pressure, with pressure elevation causing arterial constriction. The purpose of the present study was to determine whether these vessels respond in a similar fashion to changes in arterial pressure. In 39 pressure flow studies on segments of terminal ileum, resistance decreased with pressure reduction in 72% of the experiments and increased in 28%. The passive increase in resistance with pressure reduction was seen primarily shortly after the surgical procedure was completed. Thus, it appears that the resistance vessels of the intestine are not ordinarily passively distensible with changes in arterial pressure. As a result of this vascular reaction, the influence of arterial pressure on blood flow is at least partially counteracted. The mechanism of this autoregulation of flow is not a local reflex, a change in interstitial fluid volume, or a change in tone of the intestinal muscle. Changes in concentration of aerobic or anaerobic metabolites and oxygen tension of the tissues were likewise eliminated. It is concluded that autoregulation of intestinal blood flow is a result of the sensitivity of vascular smooth muscle to change in tension (a myogenic response).

Regional Variations in Uptake of Radioactive Carbon Monoxide in the Normal Lung.

C. T. DOLLERY *et alii* (*J. appl. Physiol.*, May, 1960) report that carbon monoxide labelling with ^{15}O was produced by passing ^{15}O, made in the Medical Research Council's cyclotron, over charcoal at 1000° C. After a single breath of the radioactive gas the rate of fall of activity during apnœa was measured by external counting in different regions of the lungs of normal subjects in the sitting position. The carbon monoxide clearance rate calculated from these data is proportional to the diffusion per unit volume in the zone under study. There was a gradient of diffusion per unit volume, the highest value being found in the basal regions of the lung and much lower values toward the apex. On exercise the clearance rate in the upper zone increased to a value similar to that in the lower zone at rest; the clearance rate in the lower zone was unchanged. Measurements of the ^{15}O clearance rate showed a similar gradient, but on exercise both upper and lower zone values increased so that the gradient was maintained. The results are interpreted as showing that in the resting state all the basal capillaries are open but that the proportion of patent capillaries diminishes toward the apex. On exercise there is an increase in flow at both apex and base and in consequence the remaining apical capillaries open.

On the Periphery.

CARREL, LINDBERGH AND THE CULTURE OF ORGANS.

In 1938, Alexis Carrel and Charles Lindbergh published "The Culture of Organs", a book which may one day be recognized as one of the landmarks of twentieth-century science. The achievements set out there had been dreamt of for more than a hundred years, but had never before been approached. Never before had whole organs, as distinct from cell colonies, been kept alive *in vitro* for long periods under conditions resembling those of the living body.

This aim followed logically from Carrel's views expressed in earlier works. He continually stressed the need to study the functions of organs together with their anatomical features. Moreover, their functions could be understood only in relation to their medium—the tissue fluid or lymph which consitutes the *milieu intérieur* of Claude Bernard. Obviously, then, "to study structure at the same time as function and tissues at the same time as [their] medium, we had to learn how to dissect the body, not into dead parts, but into living ones" (Carrel and Lindbergh, 1938).

Since organs were to be studied whole, the old culture methods which involved the crushing of tissues into small fragments could not be used. The answer was to circulate a nutrient fluid through the arteries, capillaries and veins of the organ.

Such a development had been foreseen as early as 1812 by Le Gallois, a French physician who wrote:

> If one could substitute for the heart a kind of injection of arterial blood, either natural or artificial, one would succeed in maintaining alive indefinitely any part of the body whatsoever.

During the last century, several workers built various devices and perfused animal muscles, kidneys, hearts and in one case even a severed head. Some success was achieved in reestablishing organ functions, but in no case did the organs survive for more than a few hours. Because they were in the process of autolysis or breakdown, no valid postulates could be made for living organs.

Carrel entered the field in 1912. To maintain a normal circulation of the excised abdominal viscera, he removed the heart and lungs with them, and then injected air into the lungs (Carrel, 1913). But the difficulty of this method convinced him that the answer lay in an artificial circulation. He joined forces with Colonel Lindbergh in 1934, after Heinz Rosenberg, another top aeronautical engineer, had failed to design a suitable perfusion pump. Lindbergh's first attempt, a sealed apparatus controlled from the outside by a system of magnets, was also a failure, as were several models that followed.

At this stage no method had been able to provide complete sterility against bacterial infection. Even the high degree of surgical asepsis which had been responsible for the success of Carrel's technique for end-to-end anastomosis of blood vessels did not suffice. Asepsis had to be supplemented by antisepsis. In World War I he had learnt the effectiveness of simple antiseptics like sodium hypochlorite. (This was the basis of the Carrel-Dakin treatment, in which wounds were washed every two hours with hypochlorite solution. Thousands of limbs which would otherwise have been amputated had been saved by this means.)

Now Carrel was able to eliminate infection of excised organs by protecting the operating field with pads soaked in hypochlorite, and by washing gloves, instruments and surgical threads in the solution.

On April 5, 1935, he first succeeded in keeping an organ alive and functioning. The following is a condensation of his description (Carrel and Lindbergh, 1938):

> A cat was bled to death under ether and the neck opened. A cannula was inserted into the lower part of the carotid artery. With a Gentile syringe Ringer's solution was injected into the artery and [therefore into the] vessels of the thyroid gland. Then the carotid was tied and cut 2 cms above the thyroid and the gland removed in mass with surrounding structures.
>
> The left thyroid was fixed in formalin and kept as a control; the right was placed in the organ chamber and perfusion started with 40% cat serum in Tyrode, using phenol red as stain, and a gas mixture of 3% CO_2, 21% O_2 and 76% N_2. After eighteen days of perfusion the right gland was about the same size as the control. A few fragments of this gland were embedded in a plasma coagulum: epithelial cell soon extensively invaded the medium, proving that the thyroid had remained alive. Sections of the glands showed a large necrotic area but many follicles were normal. The epithelium was lower than in the control and there were no vacuoles in the colloid. The idea of Le Gallois had been realised.

This was no mere scientific curiosity. Once the technique had been mastered, it was applied in hundreds of rigorously controlled experiments. All that can be attempted here is to indicate some of the methods used and results obtained.

Two main types of perfusing media were used, natural and artificial. The former consisted mostly of blood serum diluted with Tyrode's solution. Other substances such as insulin, hæmoglobin, adrenaline, pituitary hormone, protein digests and salts of potassium and sodium could also be added. Whole blood had to be treated with heparin, and even then could be used only in short experiments. Various methods were used to offset the low oxygen capacity of serum as compared to whole blood—methods such as adding hæmoglobin, subjecting the fluid to a high gas pressure and lowering the temperature and thereby the metabolic rate of the perfused organ.

Natural fluids are simple to prepare, but serum is expensive and not easily obtainable. The composition is variable and unknown. It was to remedy such faults that artificial media were introduced. These contained little or no serum as such. Some were simply digests of ox serum (Landsteiner) or blood (Baker). Others were complex solutions of chemicals, such as hæmin, cysteine, glutathione, insulin, thyroxine and various peptones, vitamins and salts. They were especially suited to the analysis of the organ's interactions with its medium; for example, the functions of serum proteins could not be studied except by cultivating an organ in a medium lacking proteins. Artificial media are far more readily available and cheaper than serum.

All perfusing fluids, of course, had to have an osmotic pressure and pH close to that of blood. They had to be filtered until completely free from foreign bodies including bacteria. Phenol red was added to enable pH changes during perfusion to be followed.

Most organs stayed alive as long as perfusion was continued—this time varied from one to forty days. The criterion of life was normal activity, so that a kidney was not taken as being alive unless it secreted urine. When serum was used, the degree of preservation varied with serum concentration. No determination was made of the longest period of life attainable *in vitro*.

Various organs showed different responses when cultivated in serum. Arteries, veins, thyroids, parathyroids, ovaries, nerve ganglia, lungs and heart remained apparently normal. However, pancreas, spleen, suprarenals and testicles were more or less altered, while kidneys degenerated rapidly, probably because of anoxia. In the case of the pancreas the acini and ducts were often well preserved, but the islets of Langerhans degenerated. Landsteiner's ox serum digest, despite its nutritional deficiencies, preserved thyroids and ovaries, though at a low level of activity.

In another series of experiments the oxygen capacity was greatly increased by retaining the hæmoglobin of whole blood but preventing clot formation, either by the use of heparin or by hæmolysis of the red cells. Kidneys and testicles were more successfully perfused with this medium than with serum.

The chemical composition of the perfusing fluid was found to have considerable effect on the metabolic activity of thyroids, ovaries, pancreas, heart and kidneys. Activity was roughly estimated from the increased acidity due to the release of metabolites, which was in turn estimated from the colour assumed by the phenol red. Another method was to find the amount of glucose removed by the organ from the circulating fluid. Witte's peptone and other protein digests were found to be strong stimulants, increasing thyroid metabolism threefold.

As the organs were subjected to varying conditions of pressure, simulating circulatory variations *in vivo*, they showed the expected reactions. With higher systolic and diastolic pressures the cells of a perfused thyroid were larger and more numerous. However, these effects were small, and could be explained by the greater flow of fluid through the organ per unit time.

Some workers since Carrel and Lindbergh have followed other paths in their efforts to cultivate organs. Much simpler and cheaper techniques use as nutrient, not perfusing fluid, but plasma coagulum, the whole being placed in

small, covered Petri dishes. Martinovitch (1951) has cultivated adrenals, gonads and pituitaries of infantile rats in this way. Gaillard (1951) has applied the method to human replacement therapy: parathyroids from full-term babies and ovaries from prematurely-born fœtuses have been kept for transplantation. But though this technique has obvious advantages and wide practical possibilities, its use in analytical experiments is very limited compared with that of the Lindbergh pump.

Thomas and his fellow-workers (1949) accepted the idea of a perfusion pump, but were not satisfied with Lindbergh's model. As they pointed out, it has many limitations: the gas mixture exerts its pressure only on the free surface of the fluid, which is small in relation to that of blood in the alveolar capillaries, so that oxygenation tends to be inadequate; the use of whole blood, desirable in order to reproduce in-vivo conditions as closely as possible, is very difficult because of the clotting factor; the apparatus is made of glass and is therefore very fragile; the size of an organ to be perfused is limited by the chamber.

By 1947, after ten years' work, they had built an apparatus free from many of these faults. All the fluid could be adequately oxygenated; the parts were of metal, not glass; the chamber size was variable, so that bulky parts like isolated heads could be accommodated; the fluid was continually changed. It also had many features of the Lindbergh pump in that pulse rate, respiration rate, systolic and diastolic pressures and stroke volume could all be varied within wide limits. However, the difficulties preventing the use of whole blood had not been solved.

The Dale-Schuster pump, developed independently of Lindbergh, is widely used in experiments, but perfusion can be continued for only a few hours.

Carrel himself realized the need for many improvements, including most of those achieved by Thomas. He also saw that a special technique was needed for cultivating parts of the central nervous system which cannot survive anoxæmia for more than a few minutes. Unfortunately the approach of World War II cut short the work of Carrel and Lindbergh.

Finally, one should consider what benefits medicine may hope to reap from the development of perfusion methods. The following is based on Carrel's own predictions, and allowance must be made for his natural optimism.

During normal life organs do not manifest all their potentialities. Their response to pathological factors, such as chemical or physical changes in the circulating medium, can be isolated and studied only when new and strictly-controlled conditions of life are created.

Many basic questions of normal physiology can be attacked. What part do the various components of serum play in the nutrition of tissues? Do all organs require plasma proteins and lipids? What organs produce the globulins involved in antibody reactions? What action do therapeutic drugs have on various organs? What factors are concerned in inflammation? What are the actual functions of the leukocytes? How does the secretion of one organ affect another?

Descriptive and causal embryology should also be extended, since embryos are easily perfused, either within the uterus or outside. In pathology, diseased organs may be studied alive.

Human adrenals, thyroid and pancreas will be allowed continuously to secrete their products into the circulating medium, which contains no foreign proteins and can therefore be safely injected into humans to remedy hormone deficiencies, at present treated with animal extracts. It will be possible to remove diseased organs and place them in the pump, "as patients are placed in a hospital". There they can be treated much more effectively than within the body, and replaced when cured. In this way a thyroid will be removed for Basedow's disease or a kidney for tuberculosis. As surgical techniques for the suture of blood vessels and other necessary operations are well developed, replantation should offer little difficulty.

But Carrel believed that the most important applications would be nutritional and not surgical. Growth, regeneration, wound healing and hormone secretion all depend on the composition of the fluid diffusing from the capillaries to each organ. It was Claude Bernard who wrote: "We will acquire a scientific explanation of these phenomena only when we can determine . . . the general condition of nutrition of all histological elements, together with the nutrient agents specific to each of these elements." For example, if the specific agents needed for normal functioning and insulin production of the pancreatic islets were found, diabetes could be treated by administering these agents, which are presumably lacking and so regenerating the islets. In fact, it may become feasible to supply the living body with the substances required for the regeneration of any organ.

Yet in the twenty-two years since Carrel expressed these hopes, few of them have actually been realized. Emphasis in research has been on the culture of tissue fragments rather than of whole organs. However, the fundamental questions for which Carrel devised his methods are still largely unsolved and just as vital as they were in his day. If, as has been suggested, he was over-optimistic and the methods cannot in practice do all that he hoped, they will nevertheless be remembered as an inspiring attempt at dissecting the human body into living parts instead of dead ones.

But if some of the results he foresaw can be realized, then the science fiction of today's medicine will become the reality of tomorrow, and Alexis Carrel and Charles Lindbergh will take their place among the great pioneers of medical history.

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Out of the Past.

THE FIGHT AGAINST TUBERCULOSIS IN SOUTH AUSTRALIA.[1]

[From the *Australasian Medical Gazette*, January 20, 1902.]

THOUGH it is only during the last few years that the crusade against consumption has had a definite and specific character, yet it has, in reality, been carried on ever since the early days of sanitary reform. A new colony begins with Arcadian simplicity, only to find, in a few years, that it is accumulating the evils of "Civilization" common to older countries. In time there comes a period of awakening, and an effort is made to get rid of evils which ought not to have been allowed to exist. Now all these efforts have been attacks directly or indirectly against tuberculosis . . . Instead of being reduced by the various sanitary reforms, the death-rate slowly mounted up till in the year 1888 it reached its climax of 1·19 per thousand, then for several years it oscillated till in 1895 it began to go steadily down, and last year with 0·84 per thousand it reached the lowest point for a great many years. It might be a matter of surprise that in England the phthisis death rate began to decline as early as 1838, when the first efforts for sanitary reform were made, reaching in that year the enormous figure of 3·8 per thousand. it gradually fell till in 1895 it was only 1·4. But it must be remembered that consumption is a disease of "Civilization" with its attendant evils of overcrowding. The effect of overcrowding had been fully felt in England as early as 1838, and as slowly but surely sanitary reforms were put into force the death rate fell. But here, the evils of civilization increased at a greater rate than legislation was able to cope with, and it is only within the last decade that it has been possible to turn the tide. It is difficult to say how far immigration affects the death rate from phthisis, but I would say that at least ten per cent. of the fatal cases are imported.

[1] From the original in the Mitchell Library, Sydney.

British Medical Association.

SOUTH AUSTRALIAN BRANCH: SCIENTIFIC.

A MEETING of the South Australian Branch of the British Medical Association was held on October 27, 1960, at the Repatriation General Hospital, Springbank.[1] Three cases were presented and discussion followed.

Multiple Myeloma.

DR. J. N. SLADDIN discussed the case of a male patient, aged 65 years, who had been admitted to the Repatriation General Hospital in July, 1960, with a two weeks' history of upper respiratory infection with pleuritic type pain in the left side of the chest. For the week prior to his admission he had had recurrent hæmoptyses, and had been treated by his local doctor for bronchitis. The examination made at the time of admission showed him to be in some respiratory distress, and he continually complained of pain in the back and the left side of his chest. He was afebrile, and the pulse rate was regular at 120 to the minute. The blood pressure was 125/75 mm. of mercury. Numerous coarse râles and rhonchi were heard over the lung fields. There was slight elevation of the jugular venous pulse. No pleuritic rub was heard, and the heart was normal on clinical examination. The liver was felt to be enlarged and tender. No lymph-gland enlargement was found. Neurological examination was normal, but movements of the lumbar part of the spine were grossly restricted because of pain.

A provisional diagnosis of congestive cardiac failure precipitated by a respiratory infection was made, and he was treated with expectorants and with diuretics given by mouth without satisfactory response. A number of investigations were performed. The hæmoglobin value was 10·1 grammes per 100 ml.; the total white cell count was 9500 per cubic millimetre. The erythrocyte sedimentation rate was 133 mm. in one hour. Examination of a blood film showed anisocytosis of the red cells and rouleaux formation. An X-ray film of the chest was normal. No pathogens were cultured from the sputum. Albumin and Bence-Jones protein were present in the urine.

Four days after his admission to hospital he developed a fever, for which penicillin and sulphamethoxypyridazine were prescribed. On the eighth day in hospital the hæmoglobin value had fallen to 7·7 grammes per 100 ml., and the total white cell count was 12,000 per cubic millimetre. The blood film showed approximately 5% of plasma cells, and the neutrophils showed a shift to the left. On the same day, examination of bone marrow from the iliac crest showed malignant hyperplasia of the plasma-cell series consistent with myelomatosis. Further investigations confirmed the diagnosis of multiple myeloma. The total serum protein content was 12·6 grammes per 100 ml. (albumin 3·0 grammes, globulin 9·6 grammes). The electrophoretic serum pattern showed the alpha level at the lower limit of normality, but with an intensely stained band in the gamma globulin region strongly suggestive of macroglobulins. The serum calcium level was 11·5 mg. per 100 ml. X-ray examination demonstrated pathological fractures of the third lumbar vertebra and the left fifth rib. Osteolytic lesions were seen in X-ray films of the pelvis, both femora, the scapulæ and the humeri. The X-ray appearances of the skull were normal.

Treatment was mostly palliative, consisting of analgesics and transfusions of whole blood. Later in his illness, the patient received specific treatment with urethane at another hospital, but continued to decline, and died on October 16, 1960.

DR. DOROTHY WHITE presented films of peripheral blood and bone marrow taken during life, showing typical myeloma cells, and gave a summary of tumour deposits in bone examined at autopsy.

Discussion.

DR. C. H. AKKERMANS: I think I have seen a recent reference to the use of radioactive iodine in multiple myelomatosis—could you comment on this?

DR. SLADDIN: Radioactive iodine has been used orally and by the intravenous route. It is thought to alleviate symptoms temporarily, but to have little effect on the course of the illness and no effect on the biochemistry of the disease.

DR. DENE HICKS: Why should urethane relieve the back pain, when the osteolytic appearances remain unchanged? I remember a patient with four collapsed lumbar vertebræ, who had been virtually bedridden for three months. After three weeks on urethane she was able to walk about the ward. This response must be common, as it was predicted by the orthopædist before treatment commenced. The woman subsequently survived for many months.

DR. SLADDIN: In our case there was no real alleviation of back pain. Perhaps he did not live long enough for this to occur. Urethane does cause changes in the pathological biochemistry, so I suppose there is no reason to suppose the osteolytic lesions themselves might not be changed, if the patient lives long enough.

DR. D. A. KENNEDY: Is there any relationship between the Bence-Jones proteinuria and the increased gamma globulins?

DR. SLADDIN: There does seem to be some slight relationship. Bence-Jones proteinuria is found in about 50% of cases, but it is more likely to be found in those cases in which the change in the electrophoretic serum protein pattern is less abnormal. There are cases in which the serum proteins are nearer normal than the case we saw here tonight. There are groups of cases in which serum proteins are quite normal. In these cases, the Bence-Jones proteinuria is more likely to be seen. One reason given is that the high and abnormal gamma globulins may themselves cause actual blockage in the renal tubules, and that this in turn will not allow the Bence-Jones proteins to be found in the urine.

DR. R. MCEWIN: How do these cases usually present? Is there any relation between the bronchitis and the final diagnosis?

DR. SLADDIN: That is a good question, and mainly the reason we are presenting this case. He presented simulating a common disease — chronic bronchitis (and perhaps a bronchopneumonia) with mild congestive heart failure. His local doctor made this diagnosis, and we agreed with it. Further questioning revealed the low back pain, present for many months. To answer your question, the commonest presenting symptom is skeletal pain, the common sites being the lumbar region and the rib cage. Although osteolytic lesions are common in the skull (but absent in this case), skull pain or headache is rare. As Dr. Hicks has said, lumbar pathology may proceed until vertebræ collapse causing actual neurological damage. This patient presented with bronchitis. I think 60% to 70% of patients suffer recurrent pulmonary infection. It is interesting to note that most of these patients have not only high gamma globulins, but abnormal gamma globulins—dysgammaglobulinæmia. Perhaps these patients lack the normal antibody response to normal globulins, and so have less resistance to respiratory infections.

DR. M. E. CHINNER: In my experience, bronchitis and back pain bring these patients along; sometimes these presenting symptoms will be present for many months before the actual diagnosis is made. In one case, we thought we had a post-menopausal osteoporosis with extreme stiffening of the lumbar spine, fish-shaped vertebræ and anæmia. Anæmia is a fairly common occurrence, as is macroglobulinæmia. This is my experience of a number of these cases.

DR. F. R. HONE: Dr. Greenway says the most common sign is tenderness on percussion of the sternum. My experience is that people with this disease present with trouble in the back and other large joints. Was there any involvement of the kidney in this case?

DR. WHITE: I saw the sections of the kidney, which showed no obstruction of the tubules at all. I agree this is commonly present, but was not seen in this case.

DR. SLADDIN: The sign of tenderness of the sternum to percussion was absent in this case. There was tenderness over the third lumbar vertebra, which was fractured. I feel we should mention the differential diagnosis at this stage. The first thing that comes to mind is secondary skeletal deposits. This reminds me that, in this case, we omitted to estimate the serum alkaline phosphatase content. It is almost always normal in multiple myeloma, in which there is an osteolytic lesion without any reactive osteoblastic formation. As Dr. Chinner has mentioned, unexplained anæmia is another common finding which must be considered in the differential diagnosis. One should also keep in mind post-menopausal and senile osteoporosis, hyperparathyroidism, lymphatic leukæmia and chronic renal disease. Regarding treatment — it is still, of course, a depressing disease, necessarily fatal; but we hope by drawing your attention and that of others to it, eventually

[1] Acknowledgement is made to the Chairman of the Repatriation Commission for permission to publish details concerning patients under the care of the Department.

we will all be looking for it, diagnosing it more often and someone will arrive at a cure. At present urethane seems the best treatment. Urethane, and to a lesser extent ACTH and cortisone, seem to be the only drugs that appear to have any effect on the course of the disease, and even so, only appear effective for a short time. Radiotherapy gives temporary palliative relief of localized skeletal deposits. Radioactive iodine has been mentioned. Radioactive phosphorus and nitrogen mustard are of little value.

DR. AKKERMANS: What is the life expectancy of a man with this condition? Is there not a condition of amyloidosis which occurs in this disease, similar to that seen in chronic suppurative disease?

DR. SLADDIN: The life expectancy is relatively short in the average case, from a few months to probably eighteen months or two years, although patients have been known to live longer. This is particularly so in cases of the so-called solitary myeloma, which have been diagnosed when the disease was in its very early stages. It has been fairly well established that the so-called solitary myeloma as such does not exist, but is merely the early stage or precursor of myelomatosis. There is a condition known as paramyloid occurring in association with this disease, but Dr. White found no evidence of this in our case. I am uncertain of the mechanism of paramyloid. In secondary amyloidosis in association with chronic suppuration (for example, tuberculosis), the distribution is mainly in the liver, kidneys and spleen. In cases of multiple myeloma, when paramyloidosis does occur, the site is more likely to be in muscle (for example, the heart, causing cardiac failure), the gastro-intestinal tract (causing hæmorrhage), and the tongue (producing macroglossia). Only rarely is paramyloid seen in the liver, spleen and kidney, but the mechanism for this deposition is unknown to me.

Medical Societies.

PÆDIATRIC SOCIETY OF VICTORIA.

A MEETING of the Pædiatric Society of Victoria was held on May 11, 1960.

Hypocalcæmia in Childhood.

DR. H. BREIDAHL discussed the case of a boy, aged 13 years, suffering from hypocalcæmia treated at the Alfred Hospital, Melbourne. He had a past history of infantile eczema, and of asthma since the age of 10 months. He had had the usual exanthemata, and two episodes of pneumonia. His schooling had been retarded by his chest troubles and by emotional difficulties. At the ages of three, six and eleven years he had had convulsions associated with febrile episodes. For the two years prior to his admission to the Alfred Hospital, he had been difficult to control at home, had refused to do any work at school, and had had episodes that were called "emotional upsets". They consisted of twitching of the right side of the face, with the left eye turning up, and of inability to walk. When he was supported, he flopped along with sagging knees. The attacks with turning of the left eye were often accompanied by a crowing noise. Four and a half months prior to his admission to hospital he started having typical epileptic convulsions. He had no further episodes after treatment with "Dilantin" and phenobarbitone, but did have further episodes of weakness of the legs. His dentition was delayed, and he suffered from enuresis. He had been referred by Dr. J. Game, who had found a lowered serum calcium level while investigating his epilepsy. The estimation had been performed because of the finding of bilateral symmetrical calcification in his basal ganglia on X-ray examination of his skull.

He was a quiet, surly boy, with a round face and irregular teeth. His height was 58 in. and his weight 104 lb. His blood pressure was 110/70 mm. of mercury. There was moderate gum hypertrophy. His hands were malformed, with shortness of the outer two fingers on both hands, and kyphoscoliosis was present in the spine. Systemic and neurological examination gave negative results, apart from the eliciting of Chvostek's and Trousseau's signs. The optic fundi were normal, although Dr. Game had previously found mild swelling of the optic discs. A number of investigations had been carried out. The serum electrolyte concentrations were: sodium, 138 mEq/l.; potassium, 3·7 mEq/l.; chloride, 92 mEq/l.; bicarbonate, 30 mEq/l.; blood urea level, 40 mg. per 100 ml. The serum proteins were normal and the cerebro-spinal fluid was normal. An electrocardiogram showed a long *Q–T* interval with low voltage *T* waves. Electroencephalography produced an abnormal record with focal outbursts over the left hemisphere, unchanged by the intravenous administration of calcium gluconate. The result of a glucose tolerance test was within normal limits. The urinary calcium excretion was 2 mg. per day. A renal function test showed that 3·3 grammes of urea were excreted in three hours. At the time of his admission to hospital (March 24, 1959), the serum calcium concentration had been 3·0 mEq/l., the phosphorus concentration 6·5 mEq/l., and the alkaline phosphatase concentration 34 K.-A. units.

Radiological investigation gave the following findings. In the chest the lung fields were clear, and the cardio-vascular outline was normal. In the hands the first, third, fourth and fifth left metacarpals were abnormally short, owing apparently to early closure of their epiphyses. The first metacarpal was shorter than the fifth. In the right hand similar changes were present in the first, fourth and fifth metacarpals. The epiphyses of the distal phalanges of both thumbs were united. There was soft-tissue calcification in the vicinity of both wrists. In the feet, both fourth metatarsals and the right first metatarsal were noticeably short. Many of the phalangeal and metatarsal epiphyses had united. There was some soft-tissue calcification at the base of the fifth left metatarsal. In the legs, apart from a number of "Harris" growth lines in the upper ends of both tibiæ, the appearances were within normal limits. In the skull, no definite basal ganglia calcification was visible, and the appearances were within normal limits. Good films of the teeth were not obtained, owing to the patient's inability to cooperate, but there was some evidence of aplasia with amputation of the roots of some teeth. In the lumbo-thoracic segment of the spine, the vertebral bodies appeared decalcified, with coarse trabeculation, and some showed concave upper and lower margins, indicating slight compression by the intervertebral discs. The renal outlines appeared normal in size and shape; no soft-tissue calcification was seen.

When the tests were completed, the patient was treated with "A.T. 10" and calcium lactate. The "A.T. 10" was initially given in doses of three capsules daily, and the calcium lactate as 14 heaped teaspoonfuls of the powder. The "A.T. 10" was increased after 10 days to six capsules a day, but after three weeks he had shown no response at all. Calciferol was then given instead, the initial dose being 150,000 units per day, increased to 250,000 units per day. It was not until one month after treatment with calciferol had been started that the serum calcium level began to rise, and after a further week it was in the normal range. His serum phosphorus level took a further month to fall to normal.

Dr. Breidahl said that the boy had since been very well, and had considerably improved mentally and socially. He was catching up with lost school work, and was improving in his behaviour towards his medical advisers. His skeletal growth was increasing towards normal for his age. His dose of calciferol was 100,000 units per day, and he was not taking calcium lactate.

DR. D. CHEEK asked whether aluminium hydroxide gel had been used to reduce the phosphate level. Regarding the Ellsworth-Howard test which had been performed, he agreed that the parathormone available was very crude.

Dr. Breidahl replied that "Amphogel" had been used, without effect.

DR. M. ROBINSON said that in vitamin D-resistant rickets, "A.T. 10" could rapidly produce hypervitaminosis D, which was slow to disappear.

Intestinal Atresia and Stenosis.

MR. DAVID SCHLICHT presented a paper based on the study of all patients with intestinal atresia and stenosis admitted to the Royal Children's Hospital between May, 1955, and December, 1958. In May, 1955, concern had been felt about the results of treatment of intestinal atresia at the hospital. In an attempt to improve the results, Mr. Murray Clarke and himself as his assistant surgeon had been given an opportunity to operate on all patients with intestinal atresia. From that date until December, 1958, they had continued to care for all those patients, and also the majority of patients with intestinal stenosis. At the onset of the project, it had been decided that all such patients would be admitted to the one ward, and that their pre-operative and post-operative management would be carried out in consultation with the physician into whose beds they had been admitted.

There had been a total of 12 patients with intestinal atresia submitted to operation, with a survival rate of 50%.

All the survivors had been followed up, and with the exception of one patient were showing very satisfactory progress. The exception was suffering from a malabsorption syndrome, owing to an extensive bowel resection. In the period 1950 to May, 1955, there had been a total of 18 patients with atresia submitted to operation, with a survival rate of 17%. In the May, 1955, to December, 1958, series, there had been three patients with atresia not operated upon, consisting of one mongoloid child and two premature babies whose condition was so poor that death occurred within twenty-four hours despite resuscitative measures. If those three cases were included, the total survival figures for all cases of intestinal atresia would be 40%. In the 1950-1955 series there had been two similar patients not operated upon, making a total for the series of 20, with an overall survival of 15%. From May, 1955, to December, 1958, there had been six patients with intestinal stenosis submitted to operation, with 100% survival. In 1950-1955 there had been five patients submitted to operation, with 100% survival.

It was therefore clear that the results of treatment of intestinal stenosis were entirely satisfactory, and that considerable improvement had been achieved in the management of intestinal atresia. A comparison of those recent results was then made with the results of two overseas series. From the Babies' Hospital, New York City, the figures for intestinal atresia from 1939 to 1955 showed a 37% survival rate. For intestinal stenosis during the same period, the figures showed a survival rate of 53%. Figures from the Boston Children's Hospital from 1940 to 1952 for intestinal atresia showed a survival rate of 53%. Since 1952, there had been 17 cases of atersia at that hospital with 70% survival.

The results of treatment of intestinal atresia and stenosis were then compared with the results of treatment of neonatal intestinal obstruction due to other causes at the Royal Children's Hospital between May, 1955, and December, 1958. In that comparison in Hirschsprung's disease there was a survival rate of 76%, in volvulus neonatorum a survival rate of 69%, in imperforate anus a survival rate of 59% and in meconium ileus a survival rate of only 8%.

Mr. Schlicht then discussed the reasons for the improved results in the management of intestinal atresia. He said that one of the most important factors had been that all patients had been nursed in the same ward. Definite advantages had accrued from the use of "Isolettes", from the improved pre-operative and post-operative electrolyte balance, and from the patients' being nursed in a ward which specialized in the nursing of premature infants. Another important factor had been improved anæsthesia. That improvement had been aided by the substitution of "Scoline" for curare, and by the firm establishment of cyclopropane as the most reliable and safe anæsthetic. The surgical management had also contributed considerably to the improved results. That had resulted, firstly, from the channelling of those cases to a specific surgical team. As a result, certain procedures had evolved. A transverse supraumbilical incision was constantly used. For duodenal atresia, a retrocolic isoperistaltic duodeno-jejunostomy was performed. For jejunal and ileal atresia, resection of the area of maximal dilatation proximal to the obstruction was carried out prior to isoperistaltic side-to-side anastomosis. In addition, a further resection of a small length of the collapsed bowel distal to the site of obstruction was also carried out, in order to guard against gangrene developing in that distal loop. Analysis of the anastomotic techniques used showed that a continuous single-layer all-coat suture of chromicized catgut had proved satisfactory. Two layers of sutures tended to reduce the stoma to a dangerously small size, and offered no significant increase in security against leakage. In making the anastomosis, two atraumatic chromicized catgut sutures were used. The anastomosis was commenced in the centre on the posterior layer, and the sutures were continued out from that central point. The short ends of each suture were tied together on that posterior layer initially. The advantages of that method of suture were that both ends of the anastomosis were treated by the same Connell technique, and that there was less tendency for one end of the anastomosis to be less expertly closed than the other. Although end-to-end anastomosis was favoured by many authorities, the relative disparity in bowel size made its execution more difficult and the resultant anastomotic stoma smaller than in side-to-side anastomosis.

Early diagnosis was of paramount importance, and a plain X-ray film of the abdomen was most helpful in achieving it. In duodenal atresia and stenosis, the X-ray appearances were quite typical. In cases of intestinal atresia with survival, the average time of operation was two and two-third days after birth in both series. In the fatal cases of intestinal atresia, the average time of operation was three days after birth in both series. That difference of eight hours between survival and death, although not great, illustrated the importance of early diagnosis.

The six patients with intestinal atresia who had died were then considered in detail. The first was a premature infant with multiple ileal atresias. At autopsy, the anastomosis was found to be intact but non-functioning, as the proximal bowel was still dilated. Dense fibrous adhesions were present in the immediate neighbourhood of the anastomosis and were the direct cause of its failure to function. Diffuse pulmonary hæmorrhages were also present. In that case, death had to be directly attributed to a complication of the operation. The second case was that of a mongoloid child with duodenal atresia. After operation, leakage had occurred from the anastomosis with the development of a subphrenic abscess. The patient died on the thirteenth day as a direct result of that complication. The third case was that of a premature infant with jejunal atresia. Failure to resect the dilated bowel at the initial operation and the overlooking of a further area of stenosis resulted in the need for a second operation. After that second operation adhesions formed, which prevented function of the anastomosis. At autopsy the anastomosis was found to be intact, but the bowel above it was still dilated. Pneumonia was also present. That infant's death could therefore be directly ascribed to a failure of operative correction. The fourth case was one of ileal atresia. There was a rupture of the anastomosis line, with the development of general peritonitis necessitating a second operation just twenty-four hours prior to death. The initial anastomosis was of the antiperistaltic variety; it should have been of the isoperistaltic type. Had it been of the latter type, possibly rupture would not have occurred. Death was a direct result of rupture of the suture line. The fifth case was that of a premature infant with multiple jejunal and ileal atresias. After resection of those areas of atresia, only eight inches of the small bowel remained. At autopsy the anastomosis was found to be intact, but the bowel above it was dilated. Pulmonary atelectasis was also present. That case had presented a hopeless problem. The sixth case was that of an infant with multiple jejunal atresias necessitating extensive resection of the small bowel so that only three feet of it remained. The infant had developed a malabsorption syndrome and died on the twenty-third day after operation. At autopsy the anastomosis was found intact, but there was some dilatation of the bowel immediately above. However, it was obvious that the anastomosis was functioning satisfactorily. The causes of death were thus mainly the direct complications of operation.

Mr. Schlicht concluded that the results of intestinal stenosis had been uniformly excellent over the past eight years; that considerable improvement had been achieved in the results of intestinal atresia due to team-work and improved facilities, but that there were no grounds for complacency when Gross of Boston could report 70% survival; and that the hope for further improvement probably lay in standardization and improved efficiency of the resection and anastomosis technique.

MR. E. DURHAM SMITH agreed with resection of the blind dilated loop. He said that for diaphragmatic atresia of the duodenum, some advocated duodenotomy and removal of the diaphragm. It was almost a routine in Boston to use a gastrostomy as part of the treatment of intestinal obstruction of the new-born, in order to avoid post-operative inhalational pneumonia.

MR. P. JONES said that merely having a gastrostomy orifice was not enough—suction had to be used. He considered that a direct attack on the obstructing diaphragm was the best treatment for diaphragmatic duodenal atresia.

MR. R. FOWLER stressed that gastrostomy should either be used or not in accordance with a definite plan of treatment. He thought that some centres in the United States used it too much.

DR. CHARLOTTE ANDERSON asked whether any of the patients who had bowel resections developed macrocytic anæmia.

Mr. Schlicht said that no blood studies had been made. The survivors included patients who had had 13 in. of ileum, 15 in. of ileum and 6 in. of jejunum resected.

The Neurological Sequelæ of Jaundice of Prematurity.

DR. J. M. GOOCH read a paper on "The Neurological Sequelæ of Jaundice of Prematurity" (see page 117).

DR. KATE CAMPBELL suggested that the smaller dosage of vitamin K in use since 1955 might be a factor in the reduced incidence of kernicterus. ABO blood-group incompatibility occurred not infrequently in premature infants and was not an uncommon cause of kernicterus. It was essential to treat jaundice before abnormal neurological signs were apparent if kernicterus was to be prevented.

Dr. Gooch replied that exchange transfusion given even after the appearance of abnormal signs did lessen the severity of kernicterus.

Dr. D. Cheek said that the administration of glucuronic acid had been proved to be of no therapeutic benefit. He thought that attention should be focused on means of binding bilirubin in the extracellular fluid rather than on removing it from the body.

DR. T. G. MADDISON said that it was not proven that the kernicterus was due to hyperbilirubinæmia in all the 25 cases. Anoxia and hæmorrhage might have contributed in some cases.

A MEETING of the Pædiatric Society of Victoria was held on April 13, 1960.

Unsolved Problems in the Treatment of Meningitis.

DR. HATTIE ALEXANDER discussed the treatment of meningitis. She said that it was interesting to observe that the preventible causes of failure to cure the frequently occurring varieties of pyogenic meningitis were the same as they had been fifteen years previously. Another factor playing a significant role in the present mortality was sudden unexplained death, often with respiratory failure, occurring despite optimal therapy. The preventible causes, although well known, still deserved emphasis. The first was failure of the clinician to keep pace with recent advances; the second was late or erroneous bacteriological diagnosis; and the third was inadequate planning of the optimal therapeutic programme for each patient.

Dr. Alexander went on to say that the age of the patient was an important consideration when one was attempting to recognize the early signs of meningeal inflammation. She therefore considered the patients in two groups—those under the age of six months, and those over that age. Most of the serious sequelæ occurred in the first group. That was due to the difficulties of diagnosis in that age group owing to the expansibility of the infant skull. With that group one had to use different criteria for lumbar puncture. If a distended fontanelle was not found, that was because the fontanelle was too small, or because dehydration was present. Signs to be looked for under those circumstances included: alternating drowsiness and wakefulness; a high-pitched cry; a staring expression; and unexplained fever in a sick infant. It was very cheering to find that with early diagnosis, the prognosis in that group was just as good as in the older age group. In the latter group the signs of meningeal irritation were more obvious, and most of the patients recovered completely. In those relatively mild cases which presented in the first twenty-four hours with a clear sensorium, there should be 100% success. A second group comprised those children who presented with fever of undetermined ætiology, and who had often had antibiotic therapy sufficient to mask the clinical features of meningitis. That group was increasing in number. A third group comprised those who, despite early diagnosis, presented in a comatose or semi-comatose condition. The cerebro-spinal fluid of those patients usually contained many organisms and there was a very low sugar level. With optimal therapy very good results could be obtained in that group, the sensorium returning to normal within twenty-four hours. There was a fourth small group of baffling cases with a high mortality; they were like the third group, but the patients had a shorter period of illness before becoming comatose. The patients remained comatose for several days, and showed widespread cerebral damage. They had severe encephalitis as well as meningitis (although there was probably a minor degree of encephalitis present in all patients with meningitis); but even in that group, despite the quick onset of coma within five or six hours and its persistence for a week or more, complete recovery might occur, although sequelæ were frequent.

Dr. Alexander then said that the next group to consider comprised those patients (of whom she had seen about a dozen in the preceding couple of years) who, despite apparently mild meningitis and optimal therapy, died unexpectedly within the first twelve hours. Type B *Hæmophilus influenzæ* was the usual causative organism in that group. Sometimes respiratory failure occurred before it became apparent that the patient's illness was due to meningitis. With regard to the pathogenetic basis of the high mortality there were two probabilities—first, cerebral œdema of such rapid onset that herniation occurred, or secondly, endothelial changes in the vessels leading to cerebritis. The group comprising those ending fatally with respiratory failure within the first twelve hours might have the same pathogenesis, or might be due to rapid liberation of bacterial products under the influence of antibiotic therapy. The cause of death in those cases of type B *H. influenzæ* meningitis was different from that in the so-called Waterhouse-Friedrichsen syndrome (in which the adrenal lesion caused only a part of the clinical picture, there being widespread endothelial damage). In those cases, meningitis led to death in the bacteriæmic stage.

The second catecory of cases in which treatment was not successful was that in which there was failure to identify the ætiological agent. One could use widely-acting antibiotic agents, but that was not optimal therapy for a particular patient. The age of the child, the duration of the illness and the treatment given were more important than the ætiological agent. The incidence of petechial skin manifestations had been 25% in pædiatric patients in a recent epidemic. It was essential that laboratory facilities be available. The organism could always be identified within one hour after the cerebro-spinal fluid from an untreated patient reached the laboratory.

There were four principles which served as guides to optimal therapy. The first was to apply the correct treatment early in the disease. The second was to eliminate the causative organism in the shortest possible time. That could be done by using two agents which worked through different mechanisms, one agent being primarily bactericidal, and by attaining an effective concentration in the cerebro-spinal fluid as rapidly as possible and maintaining it for a sufficient time to kill the organisms during their first exposure. The third principle was to reduce intrathecal therapy to a minimum. The fourth principle was to avoid agents which might injure the patient. Agents for which there was a low blood-brain barrier were the sulphonamides, chloramphenicol and isonicotinic acid hydrazide. Those for which there was a high blood-brain barrier were penicillin, streptomycin, erythromycin, novobiocin and tetracycline. Because of those facts, sulphonamides and chloramphenicol were very important agents in the treatment of meningitis. Intrathecal therapy was to be avoided, not because it was damaging, but because it was cruel to use it if it was not necessary. The great concern which had been shown regarding the danger of intrathecal therapy had not arisen from using chemotherapeutic agents in reasonable dosage. There was clearly an idiosyncrasy in some patients to streptomycin; because of that, chloramphenicol was to be preferred. In cases in which the causative organism was unknown, streptomycin was contraindicated. In 19 out of a series of 150 cases, the causative agent had not been identified; those patients had all been treated with penicillin in large doses (by the intravenous route), a sulphonamide ("Gantrisin") and chloramphenicol. The 19 children had all survived without sequelæ.

Regarding the question of subdural exploration, Dr. Alexander said that it had been reported from Boston that 50% of patients had a subdural effusion, one to two millilitres being used as the borderline. She had found that more than half the patients had an effusion of more than 2 ml., but she regarded that as a natural reaction to the disease, rather than as a complication. She adopted a conservative approach, and was prepared to continue daily subdural taps for up to three weeks. Only three or four effusions had failed to reabsorb in that period, and in those cases hydrocephalus had developed. She thought that there was no neurosurgical way of handling those effusions that nature did not cure. There was no way of knowing the true incidence of subdural effusions other than by performing routine subdural explorations, as diagnostic signs were conspicuous by their absence, although the persistence of fever and irritability was of some diagnostic help.

Dr. Alexander then said that what constituted the optimal general supportive therapy was controversial. It was usual to use saline and plenty of glucose to combat shock; steroids might be used; and if severe hypotension was present, "Levophed" or similar agents should be used. The steroids probably did no harm, but were not indicated as a routine; she used them for only three or four days, and then tapered off the dosage. How to prevent sudden deaths really was not known, although tracheostomy was essential if one wished to apply intermittent positive-pressure

artificial respiration. Cerebral œdema should be relieved as quickly as possible; the intravenous infection of urea, in which neurosurgeons had great faith, was useful for that purpose. Hypothermia was also worthy of consideration. There was some evidence that sudden death was sometimes due to water intoxication resulting from the doctor's therapeutic enthusiasm. She had been impressed by a concept of Dr. John Forbes, of Melbourne, who did not give fluid intravenously at all, but merely gave maintenance amounts of fluid by stomach tube.

DR. J. COLEBATCH asked Dr. Alexander's opinion as to the probable danger of chloramphenicol inducing aplastic anæmia.

Dr. Alexander replied that she had not had a single case of aplastic anæmia. However, it was important that in premature infants the dose of chloramphenicol should not exceed 25 mg. per kilogram per day.

DR. D. CHEEK agreed that too much fluid was dangerous in meningitis. It was his policy to give less than maintenance requirements. He was dubious about the use of urea, which tended to produce an osmotic diuresis which was harmful to the patient.

DR. R. SOUTHBY asked whether one could obtain evidence of the presence of a subdural effusion by radiography.

Dr. Alexander replied that encephalography and angiography were the only useful radiological techniques for that purpose; both were procedures that should not be lightly undertaken, and she considered that a properly done subdural tap was safer.

Clinico-Pathological Conferences.

A CONFERENCE AT SYDNEY HOSPITAL.

A CLINICO-PATHOLOGICAL CONFERENCE was held at Sydney Hospital on June 21, 1960. DR. E. HIRST was in the chair, and the principal speaker was DR. JOHN SEVIER.

Clinical History.

The patient was a male, aged 59 years, who was employed as a timber loader and lived alone. Six weeks before his admission to hospital he developed a respiratory illness with cough and chest pain, and remained away from work. After four weeks he moved to his daughter's home and was examined by the local practitioner, who diagnosed pneumonia and treated him with penicillin and a sulphonamide. At that time he was feverish, with a dry, unproductive cough and repeated vomiting. His daughter also noticed swelling of his hands and face. He was not eating and was taking little fluid, but vomiting persisted. He deteriorated steadily over the 10 days before his admission to hospital. Intermittent swelling of the face, hands and ankles was noted. Three days before his admission he developed severe pain in both knees, and the next day complained of pain in both hips. At this time he was noted to be very breathless and delirious. His temperature had been elevated for most of this time, and he had probably been passing little urine; his daughter had noticed a "black" specimen on the evening before his admission.

On his admission to hospital, the patient gave a past history of a stroke with high blood pressure eight years previously. Examination showed him to be an ill man, who was drowsy and appeared dehydrated. There was no fever. His pulse rate was 100 per minute and the volume was good; his blood pressure was 130/90 mm. of mercury. The jugular venous pressure was not elevated, and the heart did not appear enlarged. There was a possible Grade I apical presystolic murmur. The lung fields were clear, and there was moderate pitting œdema of the presacral and pretibial regions. The abdomen was slightly distended, and the liver and spleen could not be felt. Rectal examination revealed no abnormality. There were no enlarged glands, and no obvious abnormality was detected in the joints. Microscopic examination of the urine on the evening of the patient's admission revealed 40 to 60 red blood cells and 10 to 20 pus cells per high-power field, and occasional hyaline casts. *Staphylococcus pyogenes* was subsequently cultured from this specimen of urine. At that time the hæmatocrit was 26·0 per 100 ml., the white cells numbered 9500 per cubic millimetre, 94% being neutrophils, and the erythrocyte sedimentation rate was 13 mm. in one hour. The serum electrolyte concentrations were as follows (mEq/l.): sodium 135, potassium 7·9, chloride 101, bicarbonate 19·0. The serum protein concentration was 5·6 grammes per 100 ml., the albumin-globulin ratio being 1·9:3·7. Oliguria was present, only 9 oz. of urine being passed in the 24 hours after admission to hospital. A rise of temperature to 100° F. then developed. Diastolic gallop rhythm and a systolic murmur were heard in the tricuspid area, and crepitations were noted at the base of the left lung. Œdema was still present. Oliguric renal failure was diagnosed, and the patient was dialysed on the artificial kidney three days after his admission, when the blood urea nitrogen level was 213 mg. per 100 ml.

Fever continued, and improvement was evident after dialysis. X-ray examination of the chest at this stage revealed some patchy consolidation in the right middle and lower zones and in the left lower zone, suggesting an inflammatory lesion. Blood culture at this stage grew a *Staph. pyogenes* which was sensitive to all antibiotics. He was given chloramphenicol (250 mg.) and erythromycin (300 mg.) every six hours by the intravenous route, and on the following day, penicillin (1,000,000 units every two hours) was also given.

There was no improvement, even though a repeated blood culture still showed the organism to be sensitive to the antibiotics being used. Deterioration continued, anuria persisted, and he was dialysed a second time, but he died on the following day, nine days after his admission to hospital.

Clinical Discussion.

DR. SEVIER: Mr. Chairman, ladies and gentlemen. Not unexpectedly, this case is remarkable, not only for its dramatic evolution, but also for the complexities of the story as it is presented to us. We are given some benefit in that the diagnosis is provided—oliguric renal failure is diagnosed, and here our search begins. Blood culture twice showed *Staph. pyogenes*, and this organism was also cultured from the urine. Hence we may assume the diagnosis of staphylococcal pyæmia. As it now stands, it is not difficult to say what was the cause of death—oliguric renal failure and staphylococcal pyæmia. However, we are here to determine what was the underlying lesion, what brought about the oliguric renal failure and the staphylococcal pyæmia.

I propose to discuss some positive and some negative aspects of the protocol rather than deal with it in detail. Then I shall draw some conclusions and call in consultation some experts that I see in the audience with us.

We have a man of 59 years, a timber loader, presumably a heavy worker, living alone and perhaps not eating as well as he might. The whole illness occupied a period of only seven weeks—four weeks at home, two weeks with his daughter and just over one week in this hospital. This illness then took only seven weeks to end the life of a presumably healthy man. We can only presume that he was a healthy man, because all we know of his past history is that he had a stroke with high blood pressure eight years previously, when he was 51 years old. We know nothing about the sequelæ of this stroke, but he could not have been severely affected or he would not have been likely to be timber-loading. We are not given details of the examination of the nervous system, and so must assume his stroke occurred in the absence of high blood pressure, as neither cardiomegaly nor high blood pressure was found at this hospital. The ætiology of this stroke is perplexing. The absence of any residual signs is difficult to explain. There are no further details of the past history with respect to alcohol, tobacco or diet, or other illnesses, or any relevant facts about family history.

Hence, we are faced with a 59-year-old man who, six weeks before admission, developed a respiratory illness, and after one month was treated with penicillin and sulphonamides by his local practitioner, who diagnosed pneumonia. The sulphonamides may have been of significance in view of the later renal manifestations.

On admission to hospital, he was found to be dehydrated and drowsy. He had been vomiting for some time, and had taken little fluid, had passed little urine and had had some manifestations of œdema. He had been breathless, febrile and delirious. He had suffered some arthralgia in knees and hips. On arrival in hospital, he was afebrile with tachycardia, good volume pulse and normal blood pressure. There was no gross evidence of cardiac decompensation at that stage, and the heart did not appear enlarged. I feel that we must accept as significant the record of a possible presystolic murmur at the apex. Lung fields were clear of both congestive and infective processes at that stage, but

he did have presacral and pretibial œdema. Abdomen was slightly distended, although we do not know what was the cause of this distension. Liver and spleen were not felt, although they may have been enlarged. Rectal examination was negative, there were no enlarged glands and no obvious abnormalities in the joints.

We are not informed of the results of ward testing of the urine, or of any evidence of recent weight loss, which we could surely expect after an illness of this nature. Clubbing of the fingers and toes, petechiæ or Osler's nodes are not mentioned. The nature of the "black" specimen of urine passed on the evening before admission must remain a subject for conjecture, but we can probably assume that he had hæmaturia.

Initially he was afebrile, but the microurine showed hæmaturia, pyuria and casts, and later *Staph. pyogenes* was cultured from this urine. He was oliguric at this stage and developed fever, and the important findings of a diastolic gallop rhythm and tricuspid systolic murmur were made. These had not been present before, and may be regarded as variable cardiac murmurs.

He was anæmic, with a slight neutrophil leucocytosis—presumably a weak response to infection. However, his sedimentation rate was fairly low and does not provide much help. He had hyperkalæmia and acidosis, with normal chloride and sodium. His serum proteins tended to be low and the albumin-globulin ratio reversed. There was definite hypoalbuminæmia. Blood urea nitrogen was 213 mg. per 100 ml. three days after admission, and we do not know the actual rate of rise of blood urea.

He was dialysed at this stage, with little improvement, and the fever continued. At this stage blood cultures revealed *Staph. pyogenes,* and there was radiographic evidence of inflammatory changes in the lungs. These changes were probably not congestive and seem to have developed too acutely to be due to neoplasm. The staphylococcus isolated was sensitive, *in vitro,* to all antibiotics, and he was given chloramphenicol and erythromycin intravenously, and penicillin was added 24 hours later when repeated blood culture showed persistent infection. The dosage of penicillin used—12,000,000 units per day—was a large one. The lack of response to fairly adequate dosage of chloramphenicol and erythromycin would indicate poor natural defences to infection, and suggests that the renal state may have been primarily responsible for his death. There is certainly adequate evidence of gross renal disease with severe oliguria and urea retention. The question to be resolved is whether there is primary renal disease or renal impairment secondary to severe infection elsewhere. This case highlights the occasional unpredictable response of infection to antibiotics in the failure of the appropriate agent to produce any effect. There were obvious reasons in this case for not using streptomycin or vancomycin in the presence of renal failure.

The antibiotics did not help the patient, nor did the second dialysis, and he died nine days after admission. This rapid, downhill course with persisting oliguria, fever, hæmaturia, pyuria, œdema, variable cardiac murmurs, pyæmia and pneumonitis, hyperkalæmia and acidosis, leucocytosis and anæmia is compatible with a diagnosis of bacterial endocarditis. There are many other possible diagnoses, but I do not propose to discuss such examples as the collagen diseases, any of which could be invoked. We know that he had a staphylococcal septicæmia, but we do not know its origin. A more marked leucocytosis may be expected in bacterial endocarditis, but this patient was obviously in the terminal phase of a severe disease. The sedimentation rate would be expected to be higher than 13 mm. per hour to support my diagnosis. Assuming that he had bacterial endocarditis with *Staph. pyogenes* as the responsible organism, a diagnosis of diffuse glomerulonephritis secondary to this is quite compatible, occurring nearly as often as a focal glomerulonephritis, and I feel that this was the mechanism of his renal failure. Certainly we could consider a long-standing pyelonephritis, but he was not hypertensive when seen at this hospital; his normal blood pressure could have been associated with a failing heart, but I feel that we should accept this as his true blood pressure, especially as he did not have cardiac enlargement, on admission. Hence my diagnosis is bacterial endocarditis with a probably diffuse glomerulonephritis and possibly some pyelonephritis. This has been associated with inflammatory lung changes without any lung abscesses, as often seen in staphylococcal pyæmia. I feel that the relatively low sedimentation rate is a strong factor against such collagen diseases as polyarteritis nodosa and disseminated lupus erythematosus. Brucellosis is an infective process worth including in the differential diagnosis, but it is less common than bacterial endocarditis. It could give rise to a picture similar to this case.

I will leave further discussion to members of the audience, my diagnosis being bacterial endocarditis with staphylococcal septicæmia and diffuse glomerulonephritis, with perhaps pyelonephritis as well.

DR. HIRST: Have we any evidence about the stroke and the examination of the central nervous system?

DR. P. CASTALDI: The central nervous system examination was negative. Reflexes were equal, and there was no change in power or tone and the plantar responses were flexor. The urinalysis revealed one-half protein and specific gravity of 1010. There was no mention made at the time of any petechiæ, splinter hæmorrhages or nodes or clubbing of the fingers.

DR. HIRST: Dr. Walsh, would you comment on the sedimentation rate?

DR. R. J. WALSH: I cannot understand the sedimentation rate with the quoted albumin-globulin ratio of 1·9:3·7.

DR. HIRST: I would like to call for comments first from the students.

A STUDENT: I think the diagnosis of bacterial endocarditis seems the most likely.

DR. FERGUSON: The sulphonamide received in the early part of the illness could be considered as an ætiological factor in the renal disturbance, especially with the subsequent history of dark urine.

DR. SEVIER: I do not think that the sulphonamides could be blamed. There was no history of rash to substantiate the possibility of sulphonamide sensitivity, although the arthralgia and œdema could have been manifestations of this.

DR. DAVID READ: One aspect to be decided is whether his renal disease was acute or chronic. The evidence for chronic renal disease seems to be lacking; there was no cardiomegaly or hypertension, although he is said to have been hypertensive previously. The fact that he was not hypertensive on this occasion probably could not be attributed to dehydration. Crystallization of sulphonamides and renal papillary necrosis following prolonged ingestion of phenacetin are other possibilities to be mentioned, but without much supportive evidence. Goodpasture's syndrome, in which glomerulonephritis may occur in association with severe idiopathic hæmorrhagic and interstitial pneumonitis, deserves a mention as a very remote possibility, although there is no history of hæmoptysis in this patient.

DR. HIRST: Dr. Read, you thought that there might possibly be chronic glomerulonephritis in spite of the blood pressure not being elevated.

DR. READ: I thought this patient may have acute glomerulonephritis with anuria and perhaps associated pulmonary hæmorrhage.

DR. R. B. GOLDRICK: I agree with the diagnosis of bacterial endocarditis, but I do not agree about the lack of evidence for chronic renal disease. The fact that a man of 51 had a stroke is significant, and is usually associated with hypertension. The absence of hypertension on admission to hospital could be attributed to dehydration due to vomiting—the comment on pulse volume does not exclude dehydration. The basis of the problem was not the bacterial endocarditis, but the nature of the renal lesion, and I think that that lesion may have been chronic pyelonephritis or chronic glomerulonephritis, and he may have had pneumonia and pleurisy complicating that disease and precipitating oliguric renal failure due to vomiting and dehydration. Secondary staphylococcal septicæmia with endocarditis preceded death.

DR. H. M. WHYTE: We could propose that this patient had a respiratory illness, which could have been due to multiple pulmonary emboli. His chest pain could have been the result of myocardial infarction which caused his blood pressure to fall, and repeated pulmonary emboli could have occurred. It is also possible that his renal disease developed as a result of the penicillin or sulphonamide given for a supposed pulmonary infection. Repeated vomiting, perhaps precipitated by sulphonamide, could have caused dehydration which led to tubular necrosis and renal failure. The origin of the staphylococcal septicæmia is not very evident. However, I would agree that he probably had chronic renal disease, and his original hypertension could have been due to this. We could also explain the low blood pressure found in this illness by suggesting a recent renal vein thrombosis with heavy proteinuria leading to low serum albumin.

DR. B. R. M. HURT: I thought that this man probably had chronic renal damage. I do not think the previous history of hypertensive cardio-vascular disease can be discarded. I am not surprised by the low blood pressure found here, in view of the staphylococcal septicæmia. Bacterial endocarditis seems established in the presence of changing heart murmurs. Management of this patient presents many problems. Could he have been saved if his infection had been overcome? I think it is unlikely that he could have survived if he did have chronic renal disease and developed a low blood pressure after the development of staphylococcal septicæmia. The reversed albumin-globulin ratio, anæmia and poor leucocyte response show that he had very little resistance to infection. A staphylococcal pneumonia could have been the reason for the septicæmia. I wondered whether his knee and hip pain could have been due to aortic thrombosis.

DR. K. B. NOAD: I think this patient had a staphylococcal pneumonia in the presence of low resistance due to poor nutrition, as suggested by Dr. Sevier. The arthralgias were non-specific in such an infective illness, and I agree with the suggestion of chronic renal disease. The previous statement of hypertension must be accepted, and although his stroke was obviously not a hemiplegia, its occurrence could be accepted. He probably had nephrosclerosis, incipient renal failure and developed staphylococcal pneumonia and septicæmia and pyelonephritis which precipitated renal failure. I would be surprised if no cardiomegaly was present, and I feel that the blood pressure of 130/90 was an expression of his failing circulation, and that he did have hypertensive cardio-vascular disease initially.

DR. W. L. CALOV: I would like to comment only on the history of a stroke. Everyone seems to consider that he really did have such an episode with associated high blood pressure. However, this depends on the daughter's report. It was probably not a cerebral thrombosis, as one would expect some residual paresis. It also was not an embolus, as this also would have left residual defects. A hypertensive attack with temporary hemiplegia or paresis could have occurred. Finally, the possibility of there being no hypertension and merely a simple Bell's palsy must be considered. It is quite common for patients or their relatives to confuse a stroke and simple Bell's palsy.

Pathological Report.

DR. A. A. PALMER: The body was that of a fairly well nourished man weighing 130 lb. There was a bed sore penetrating through the skin and measuring 10 by 8 cm. over the left side of the sacrum. Muscles, bones and joints appeared normal. No abnormality was noted in the mouth. In the pharynx was some dried blood and superficial slough of the mucous membrane. The thyroid gland appeared normal; the parathyroids were not seen.

Thorax and mediastinum appeared normal. At the bifurcation of the trachea was a mass of thick mucopurulent sputum extending down into the origins of the bronchi on both sides. The thymus was not seen. No abnormalities of the breasts were noted.

Each pleural cavity contained about 20 oz. of straw-coloured fluid. There were no adhesions and no fibrinous pleurisy.

The lungs were similar—the right weighed 27 oz. and the left 30 oz. There was some generalized œdema; the lower lobes were congested. There was no evidence of bronchopneumonia, and there were no abscesses or infarcts.

The pericardial sac contained about 3 oz. of straw-coloured effusion. There were multiple small subepicardial hæmorrhages. The mitral valve admitted two fingers, and there was a single vegetation 1 cm. in diameter on one cusp. The tricuspid orifice was narrowed by large, firm, white vegetations, involving all the cusps. There was little erosion of the cusps. The aortic valve was competent, and its cusps appeared normal. The aorta showed advanced atheroma. The renal arteries showed atheroma, but were not severely narrowed. The inferior vena cava and renal veins were not thrombosed.

The abdomen contained about 40 oz. of straw-coloured ascitic fluid. There were several ecchymoses on the peritoneal surface of the small intestine. The peritoneum appeared otherwise normal. The liver showed small changes of chronic venous congestion. The gall-bladder appeared normal.

The spleen was congested, and showed one infarct which was softened in places.

The kidneys were similar. They were large, congested and soft in consistency. The perinephric fat was easily separated, and their capsules stripped with some difficulty leaving a finely granular surface. Beneath the capsule were multiple punctate hæmorrhages, and these could also be seen on the cut surface. Several small, yellowish areas about 2 mm. in diameter were seen, suggesting small abscesses. The renal pelvis appeared normal, and ureters and vessels showed no abnormality.

There were no significant changes in the œsophagus, stomach or intestines. No abnormality was noted in the pancreas or suprarenals.

In the pelvic retroperitoneal tissue, to the left of and behind the rectum and bladder, was a shaggy but thin-walled abscess cavity containing about 10 oz. of thin, brownish, purulent fluid. The bladder contained about 4 oz. of urine, and its mucosa appeared normal. Prostate and testes appeared normal.

There was a thin layer of subarachnoid hæmorrhage spread over the occipital region of the cerebral hemispheres and down on to the cerebellum. There were several dark spots in the cerebral cortex, suggesting mycotic aneurysms. No abscesses were found in the brain.

Microscopic Examination.

Heart: The vegetations on the mitral and tricuspid valves show numerous colonies of cocci (*Staph. pyogenes* was cultured from a heart valve). There is considerable destruction of the cusps.

Kidney: Almost all the glomeruli are abnormal, and many show epithelial crescents and abnormally cellular and digitate tufts. Hyaline, cellular and red-cell casts are present in many tubules. There are some minute foci of hæmorrhage and acute inflammation. No significant arteriolar disease has been found. The changes are those of severe subacute glomerulonephritis with a few small embolic lesions in addition.

Brain: There are small hæmorrhages in which Gram-positive cocci can be found.

Summary of Autopsy Findings.

1. Subacute diffuse glomerulonephritis with oliguria and uræmia.
2. Acute bacterial endocarditis, due to *Staph. pyogenes*, involving the mitral and tricuspid valves.
3. Subarachnoid and small cortical hæmorrhages attributable to infected emboli.
4. Splenic infarcts.
5. Pelvic abscess.
6. Pulmonary congestion and œdema.

Medical Matters in Parliament.

HOUSE OF REPRESENTATIVES.

THE following extracts from *Hansard* relate to the proceedings of the House of Representatives.

December 7 and 8, 1960.

Aborigines.

MR. BEAZLEY asked the Minister for Territories, upon notice:

1. Has a survey ever been undertaken of the physique of aboriginal schoolchildren with respect to height, weight, nutrition, strength, eyesight, hearing, teeth and freedom from skin diseases, especially in comparison and contrast with schoolchildren of European origin?
2. If so, what were the results of the survey?
3. If no such survey has been made, can one be undertaken?
4. Has an educational and social survey been made of aboriginal schoolchildren with respect to (*a*) the cultural level of the homes from which they come and (*b*) the stability of the family background?
5. What is the strength of the staff of the Territory administration which is charged with aboriginal welfare, and in what respects is it so responsible?

MR. HASLUCK: The answers to the honourable member's questions are as follows:

1 and 2. I am able to answer in respect of the Northern Territory only. Survey work undertaken in this field included—

(*a*) A specific survey of anæmia and nutritional disease in aboriginal children, including a study of the mean size and weight of children and a comparison of these factors with comparable data for children of European origin, was undertaken by Dr. J. M. Crotty in the northern part of the Northern Territory in 1958. The survey showed that there was little difference in the comparison of the mean height of the two groups of children, apart from the fact that European children in the 0 to 4 years groups appeared of greater height than aboriginal children, but this difference was overcome by the age of twelve years. With regard to mean weight, it was found that the average European child up to the age of 12 years was heavier by a figure varying between 10 per cent. and 20 per cent. in the different age groups.

(*b*) Periodic surveys, including studies of growth pattern of aboriginal children and progressive changes in their dental condition after introduction of European foods, have been conducted since 1951 at selected welfare settlements by the Department of Anatomy and the Dental School of the University of Adelaide. These studies consist of observations to be carried out over a long term before final conclusions are reached.

(*c*) A comprehensive investigation of the health of children at Port Keats Mission was made by Dr. Kearns in February, 1958. His findings on height and weight showed a similar pattern to those of Dr. Crotty.

(*d*) In 1948 the Nutrition Unit of the American-Australian Scientific Expedition to Arnhem Land studied the physique of aboriginal family groups at four centres in Arnhem Land. The results have recently been published in the second volume of the records of the Expedition. The general conclusion reached was that the state of nutrition was satisfactory.

(*e*) In 1957, Doctors Crotty, Ida Mann and McLean carried out investigations of Australian aboriginals (including children) at Groote Eylandt, Oenpelli and Goulburn Island affected with trachoma. The type of trachoma found was mild with a few or no symptoms. Attempts to isolate a virus were unsuccessful.

(*f*) About half of the aboriginal population was examined in a mass chest radiography survey of the Northern Territory population conducted by the Anti-T.B. Association of New South Wales in 1959 at the request of the Commonwealth Department of Health. No separate results of aboriginal schoolchildren have been published. Generally the total incidence of active pulmonary tuberculosis was rather less than expected.

(*g*) In 1951 Miss Winifred Wilson surveyed the dietary intake of aboriginals living on missions and cattle stations. No assumptions about nutritional states were attempted in this survey. The result took the form of a guide to rationing which formed the basis of ration scales. Work in this field has been continued by the Senior Dietitian of the Department of Health who regularly visits missions and welfare settlements to study nutrition and advise on problems.

(*h*) General examinations of aboriginal schoolchildren including the state of nutrition, eyesight, hearing, teeth and skin condition are made at regular intervals by school medical officers in the case of children who attend schools in town areas, and by medical officers engaged in native survey duties in the case of children attending schools at missions and settlements. A programme of preventative dentistry is carried out continuously by visits by mobile dental clinics to missions and welfare settlements. No specific comparisons of the results of these examinations of European children have been made.

3. See answer to 1 and 2. The possibility of a comparative study of the conditions of aboriginal and European children as disclosed by school medical examinations will be considered.

4. Inquiries in this field have been made from time to time for the purpose of preparing curricula for the special schools conducted for aboriginal children. The staff of the Administration Welfare Branch is continually making observations in this field in the course of their work.

5. Two hundred officers in the Northern Territory Administration are employed solely and directly in aboriginal welfare work. The servicing organization of the Northern Territory Administratfon also serves the needs of the officers engaged in aboriginal welfare and of the aboriginals themselves. Beyond this the Department of Health, to a considerable degree, and other agencies such as the Department of Works, Agricultural Branch, Forestry and Timber Bureau, Animal Industry Branch, and Water Resources Branch all make an appreciable contribution through their work to aboriginal welfare. The head office (Darwin) cadre of the Welfare Branch in policy development, research and programming of work, and provision of services, makes a specialized contribution in fields such as employment, education, recreation, health and hygiene and social welfare, generally. District welfare officers in Darwin, Katherine, Tennant Creek and Alice Springs are responsible to see that the day to day business in aboriginal welfare in their districts is discharged effectively and efficiently and in the spirit of an active social training programme for aborigines in the Territory. Patrol officers moving through the district and resident staff on government settlements, including school teachers, nurses, farmers, carpenters, etc., maintain close personal contact with aborigines.

Pharmaceutical Benefits.

MR. MURRAY: I desire to ask the Minister for Health a question. Now that the revised pharmaceutical benefits scheme has been in operation for some months, will the Minister say whether the objectives aimed at by introducing the 5s. charge for prescriptions have been realized? Do the results achieved by the provision of pharmaceutical benefits under the *National Health Act* justify the heavy cost involved?

DR. DONALD CAMERON: The answer to the question as to whether the objectives have been achieved is, unequivocally, "Yes". One of the main objectives sought by the Government was to ensure that in such a measure as this, which is of course a social welfare measure, the recipient would bear directly some portion of the cost. Coupled with that was the desire that the very rapidly rising annual cost of pharmaceutical benefits should be in some way restrained. It is too early yet for us to give definite figures about the financial result, but I am sure it is perfectly true to say that without this measure the expenditure on pharmaceutical benefits within this financial year alone would have been several million pounds more than in fact it will be

The honourable gentleman's second question as to whether the expense is in any event justified can also be unequivocally answered in the affirmative. As I said, this is a social welfare measure. It brings a very great range of drugs within the financial resources of the population. Every national health scheme must have, as one of its objectives, the provision of adequate modern therapy for the citizens of the country. The average price of prescriptions dispensed under the pharmaceutical benefits scheme is about 19s. and with important drugs, of course, the price to the patient without this scheme would be very much greater, amounting to many pounds per prescription in some instances. In no instance does the patient under the pharmaceutical benefits arrangements pay more than 5s. So I think this can fairly be described as a social welfare measure of very great importance and, from the health point of view, of very great advantage.

MR. BURY: My question is addressed to the Minister for Health. Is the Federated Pharmaceutical Service Guild of Australia the body which negotiates with the Commonwealth Government on matters concerning pharmaceutical benefits? Does this body or its State branches accept royalties or commissions from the manufacturers of certain patent medicines, in return for which it permits the term "A Guild Product" to be used by one manufacturer only of each product, thereby conferring on such firms a very considerable commercial advantage? If so, is this a restrictive practice which effectively curtails competition and thus increases the price which the public have to pay for essential drugs? Does this practice in any way affect the cost to the taxpayers of the extensive pharmaceutical benefits which they now provide for themselves through the agency of the Commonwealth Government?

DR. DONALD CAMERON: The Federal Pharmaceutical Service Guild of Australia does negotiate with the Federal Government over the price which the Government pays to the individual chemist for pharmaceutical benefits. As the honourable gentleman will realize, the Government is concerned only with drugs which are listed as pharmaceutical benefits. The chemist is paid under a rather complicated arrangement which covers his cost of purchasing the drug, his cost of prescribing, and so on, in order to arrive at a fair price which the Government will pay to him. The honourable gentleman used the words "patent medicines".

I am not quite sure whether he intends that term to be taken in the strict sense.

MR. BURY: No—generally.

DR. DONALD CAMERON: Patent medicines are not included in the list of pharmaceutical benefits. Whether the Pharmaceutical Service Guild receives royalties on certain products, I do not know. I do not think that whether it does or not makes any difference to the price that the Federal Government pays, because that price is calculated on the actual cost of the drug—what the chemist has to pay for it—and is reviewed in the light of what the negotiators who act on behalf of the Department of Health consider to be a reasonable price. I am not sure whether the practice referred to by the honourable gentleman can be described as a restrictive practice. Whether it can or not, the matter appears to me to be outside the administrative orbit of the Federal Government. In any event, so far as I can see, the practice is unlikely to exert any influence on the price paid for pharmaceutical benefits.

Health and Medical Services.

MR. JONES: I preface a question to the Minister for Health by saying that, from time to time, people contract diseases which require operations which cannot be performed by the medical profession in Australia and the patients have to go overseas. Will the Minister, in these cases, consider making an allowance equivalent to the expense which the Government would meet in respect of hospital accommodation, medical attention and pharmaceutical preparations for these people so as to assist them in the great expense of having to go to other countries to have an operation performed?

DR. DONALD CAMERON: The honourable gentleman has raised this matter with me previously. I think that there must be very few instances indeed of people having to leave Australia because adequate surgery is not available for them here. I think I should say that the Department of Health has no funds at its disposal for the purpose of giving effect to the suggestion of the honourable member. However, if he has a specific case in mind I shall certainly have a look at it.

Medical Benefits Funds.

MR. LUCHETTI: Has the Minister for Health seen a statement which was published by the Medical Benefits Fund of Australia Limited which reveals that it has assets exceeding £2,700,000 and a claims reserve of £2,706,300? Will the Minister institute an investigation into the operations of all organizations that are registered under Commonwealth legislation to ascertain administrative costs, reserves and other assets to ensure that the insured receive benefits more in keeping with their contributions?

DR. DONALD CAMERON: The financial operations of the benefits funds are constantly under review and the Department of Health is constantly in consultation with the organizations. It would be unfortunate if the impression were gained that because some of these organizations have considerable reserves they should increase their payments to contributors. After all, if the honourable gentleman considers the position of other insurance companies he will realize that every sound insurance business must build up considerable reserves if it is to function efficiently.

Correspondence.

THE NEW SOUTH WALES STATE CANCER COUNCIL: CANCER INVESTIGATION PROGRAMME.

SIR: The present programme of cancer investigation at the Special Unit for Investigation and Treatment, located at the Prince of Wales Hospital, Randwick, requires the tissue of one of the following tumours—namely, chondroma, chondrosarcoma or chordoma—in order that enzymatic and chemical studies may be carried out on such a tissue as part of the general programme of research at the Unit. These growths are not common, but are the ones most suited to this purpose, and the object of this letter is to seek the cooperation of any surgeon who operates on a patient with one of these tumours, to make the tissue available to the New South State Cancer Council's research workers at the Special Unit. We would prefer to obtain the tissue in the fresh state within one or two hours of operation at the most. If this is not possible it should be snap-frozen and, when frozen solid, be packed in dry ice in a vacuum jar. This would keep it in proper condition for approximately 24 hours.

In the event of an operation on one of these tumours being decided upon, it would be greatly appreciated if the surgeon would communicate either with me (telephone BL 1894, Sydney) or Mr. J. B. Adams, M.Sc. (telephone FX 1121, Special Unit), when we would make arrangements to attend at the hospital concerned at the time of operation so that immediate delivery of the tissue could be taken.

The availability of such a tumour forms an important part of our investigation, and any help which we can receive would be very greatly appreciated by Council.

Yours, etc.,

ALAN B. LILLEY,
Medical Director.

The New South Wales State Cancer Council,
Challis House,
10 Martin Place,
Sydney.
January 4, 1961.

"THE JUBILEE BOOK OF THE SYDNEY HOSPITAL CLINICAL SCHOOL."

SIR: On completion of reading Dr. E. H. Stokes' pioneering compilation "The Jubilee Book of the Sydney Hospital Clinical School" (reviewed MED. J. AUST., September 3, 1960), as a former Sydney Hospital student I would like to say, if I may, how clearly and comprehensively Dr. Stokes has presented to us a picture, a moving picture in both senses of "moving", of the history, growth and development to maturity of Sydney Hospital, the earliest teaching hospital in Australia and the second clinical school of the University of Sydney. I would also like to comment upon the excellent presentation of Dr. Stokes' book by the publishers.

As your reviewer so well said: "All who are interested in Sydney Hospital will want to have this book, not only to read once, but to keep for purposes of browsing and reminiscing over the years."

I hope that this book will inspire other distinguished clinical teachers, in other Sydney teaching hospitals, to emulate the thought and labour of Dr. Eddie Stokes.

Yours, etc.,

ARTHUR D'OMBRAIN.

B.M.A. House,
135 Macquarie Street,
Sydney.
January 3, 1961.

A STUDY OF SUBDURAL HÆMATOMA.

SIR: Chronic subdural hæmatoma is a common condition, and its correct diagnosis is very rewarding. Mr. Miller and Mr. Bleasel (MED. J. AUST., December 31, 1960) have given an interesting summary of the clinical findings in their series, which will be welcomed by everyone concerned with this versatile disease. Nevertheless, certain aspects of their study are surprising. Not all surgeons will agree that "there is no marked difference between the clinical findings" in the fluid effusions and the solid clots. I have been impressed by the profound differences between these groups; the solid clots usually present as acute emergencies, more fulminating and much more lethal than extradural hæmatomas, whereas the fluid effusions present more insidiously, and commonly with the syndrome of posterior tentorial herniation. The acute, usually solid, clot tends to cause lateral cerebral compression, with rapid deepening of unconsciousness and ipsilateral pupillary dilatation. The chronic fluid effusion may masquerade in many guises; very typical, however, are the findings of fluctuating stupor with impaired conjugate gaze upwards and bilateral ptosis. It is remarkable that Mr. Miller and Mr. Bleasel have not recorded these characteristic ocular signs; in a series of 75 cases studied personally, they were present to varying degrees in 10 patients. Presumably they represent mid-brain compression by a posterior herniation; unless their significance is grasped, an erroneous diagnosis is likely.

The pathological distinction made by Mr. Miller and Mr. Bleasel between solid and liquid effusions may be valid, though I think this is debatable; my own small experience has supported the classical belief that the solid clots progressively liquefy with age, and I have more than once

followed the transition in successive operations on the same patient. Admixture of cerebro-spinal fluid may also determine liquidity. However, from the diagnostic viewpoint, surely the fundamental distinction is between the acute post-traumatic hæmatoma, usually but not invariably solid, and the chronic effusion, usually but not invariably fluid. The clinical signs seem to depend much more on the rate of evolution than on the physical properties of the hæmatoma. So also, as Mr. Miller and Mr. Bleasel clearly indicate, does the prognosis.

Yours, etc.,

254 North Terrace, Adelaide.
January 6, 1961.

DONALD SIMPSON.

AN AUSTRALIAN MEDICAL ASSOCIATION.

SIR: I am pleased that other doctors are supporting Sir Henry Newland, who has given many good reasons for choosing the name Medical Association of Australia rather than Australian Medical Association. It is not uncommon for steering committees to make errors of judgement on matters like this, and they should not be blindly followed. Our officials travelling abroad would very soon regret the worldwide identification of A.M.A. with the American Medical Association. The adoption of A.M.A. means agreeing to an inferior status in perpetuity and to the loss of our medical national identity. A senior member like Sir Henry Newland, who has had much experience in international medical affairs, is able to see this more clearly than those excellent men who have the courage to undertake a thankless and long overdue task on the home front.

Yours, etc.,

410 Albert Street, East Melbourne.
January 9, 1961.

MICHAEL KELLY.

BOWEL HABITS OF YOUNG BABIES.

SIR: Thirty-five years ago I was taught that four stools a day in new-borns was not excessive, and that by the age of three or four months a baby should have formed the "daily habit".

During the past few years, successive sisters in charge of our local infant welfare clinic have taught mothers not to bother if their breast-fed baby did not use the bowel for five or seven days. Apparently this teaching does not apply to babies given dried milk or condensed milk. Considering that all well-known brands of milk for infants are of a composition very similar to that of human milk, I fail to see any reason for allowing such a difference in the bowel habits of breast-fed and bottle-fed babies. Certainly I have observed a good few breast-fed babies with severe intestinal colic, convulsions, anorexia with failure to gain weight satisfactorily, anal fissure with aggravation of constipation, and many peevish, pasty-looking babies. All these babies promptly improved with treatment directed to the development of daily defæcation.

Surely a constipated baby is predisposed to intussusception, hernias, prolapse rectum, and later to chronic constipation with all its evil effects.

I trust an experienced pædiatrician will discuss this subject in a subsequent issue of the Journal.

Yours, etc.,

Wyalkatchem, Western Australia.
January 3, 1961.

A. M. FRATEL, M.R.C.S. (England).

ABORIGINES AND LEPROSY IN WESTERN AUSTRALIA.

SIR: Section 10 of the *Native Welfare Act* 1905-1954 of Western Australia reads as follows:

> In order that the spread of leprosy within the State may be limited the following provisions shall operate and have effect, that is to say . . . . Subject as hereinafter otherwise provided, no native who at the time of the commencement of this section is living north of the boundary line (the twentieth parallel of south latitude) or who at any time thereafter shall have passed to that part of the State north of the boundary line, shall pass to any part of the State south of the boundary line, by land, sea or air save and except in any of the circumstances following, namely . . . where the native travels in a part of the State south of the boundary line as the employee of or in company with any person droving stock . . .

It is to be noted that this legislation is worded in such a way that the squatter shall not be deprived of aboriginal labour (blatant lobbying). This is unadulterated colour-prejudice legislation. If this were not so, such legislation would appear in the section dealing with infectious diseases in the *Health Act*. Such legislation would then affect black and white alike.

In 1958, Dr. Henzell, the Commissioner of Public Health in Western Australia, was reported as saying that with the new treatment available for leprosy the number of patients in the Denby leprosarium had decreased considerably in the previous five years. It is doubtful whether any legislation on this question is required at all. If it is required, then surely legislation more in keeping with modern medical thought could easily be introduced eliminating the "leper line" and having no bias towards skin colour.

Yours, etc.,

366 Church Street, Richmond, E.1, Victoria.
January 2, 1961.

BARRY E. CHRISTOPHERS.

SIR: Dr. Christophers makes it appear that the native is allowed to cross the boundary line only for the purpose of droving stock for his employer. This is not so, and had Dr. Christophers published the whole of Section 10 and not carefully selected extracts from it, he would have demonstrated clearly that the purpose of the line is to protect natives and is not an act of discrimination against them.

A native may receive a permit to come south of the boundary line for reasons of employment other than droving, for health reasons, for education and welfare purposes, etc. The reason for the permit is to ensure that he is medically examined before proceeding into leprosy-free country and that he is available for medical surveillance for a suitable period after coming from the north.

The boundary line is a quarantine measure applied to prevent the spread of leprosy, endemic in the north, to the large groups of natives south of the line. The prevention of the spread of leprosy in this State is a problem almost entirely involved with natives, and consequently there is no justification in applying this quarantine restriction to whites.

The decrease in the incidence of leprosy is largely brought about by such control measures, and it would be iniquitous to reduce such controls and expose further areas with large native populations to infection at a time when the incidence of the disease is being greatly reduced and we can look forward to its eradication.

Yours, etc.,

W. S. DAVIDSON,
Acting Commissioner of Public Health.
Department of Public Health
57 Murray Street,
Perth, Western Australia.
January 13, 1961.

TREATMENT OF SERIOUS INFECTIONS.

SIR: I am prompted to write this letter by your leading article of January 7, 1961, entitled "Treatment of Serious Infections". The writer is obviously unaware that in rural areas antibiotics are "splashed-around" haphazardly to a degree that makes doctors' prescriptions "a drop in the ocean".

Penicillin G can be bought over the counter of the local store by farmers for use on their animals (and also themselves at times), on indications which they themselves decide. It is bought in large quantities. Mostly it is used topically, or in insufficient dose for an insufficient time. Sulphonamides have been used extensively for veterinary purposes for a long time now.

Nowadays, "poddy-calves" are being fed "Terramycin" as a routine, and this drug is being given to cattle with

increasing frequency. "Chloromycetin" is being used for topical veterinary treatment, and recently I even struck a young heifer who was "on" "Chloromycetin"—hydrocortisone eye ointment.

Some six months ago a swab taken from one of my patients showed an organism sensitive to penicillin—a most unusual surprise. I would suggest that before the writer of January 7's leading article hangs notices in doctors' waiting rooms, he finds out what can be done about the haphazard use of readily available veterinary antibiotics.

Yours, etc.,

GEOFFREY A. RICKARBY.

Muboa North,
South Gippsland,
Victoria.

CONSCRIPTION OF MEDICAL OFFICERS.

SIR: A letter written by the Secretary of the Hospitals Commission of New South Wales to a fellow recent graduate in medicine reads as follows:

> Dear Sir, The Commission has been informed by the Committee charged with the responsibility for the allocation of graduates at the recent final examinations in medicine at the University of Sydney, to various public hospitals in the State, that you were allocated to the ——— District Hospital.
>
> It has been informed by that hospital that you have intimated that you are not prepared to accept such an appointment, and are interested in taking up a similar position at another public hospital.
>
> I have to inform you that should you not accept the position at ——— District Hospital, to which you have been allocated, the Commission will not be prepared to approve of your appointment at any other public hospital in New South Wales.

This flagrant threat of "industrial conscripition" will, no doubt, outrage the feelings of all reasonable men. It is hoped that the British Medical Association and other authorities, in whose hands the future freedom of the profession lies, will move promptly and strongly to prevent further action of this kind. Not the least unsavoury aspect of the Hospitals Commission's attitude is that an attempt has been made to bully and "push around" a most junior member of the profession at the very threshold of his career.

Yours, etc.,

R.M.O.

Sydney.
January 10, 1961.

UTERINE RUPTURE.

SIR: I thought that some of your readers might be interested to hear of two unusual cases of uterine rupture. One of these ruptures occurred in labour, and the other one at the seventeenth week of pregnancy.

In this country, as in so many other countries throughout the world today where there are few midwives, and where, in consequence, only a minority of mothers receive antenatal care and intra-partum care, rupture of the uterus is frequently seen; and most of the varieties met with have been described by Professor Naguib Mahfouz in his classic Atlas, and also by Professor Munro Kerr and other writers. However, the two cases I have encountered recently are quite out of the common run and perhaps are worthy of being reported in your Journal.

Case I.

This was an Ethiopian woman, aged 35 years, who had had two previous Cæsarean sections (lower segment) performed for obstructed labour. She came to this hospital as an emergency late in her next labour, complaining of loss of fœtal movements and of "exhaustion". She had been in strong labour at her home in the country some distance from Addis Ababa for 20 hours. The signs of ruptured uterus were so obvious at a glance that we had no hesitation in operating at once, expecting, of course, to find that the scars of the two previous Cæsarean operations had given way. When we opened the patient's abdomen, we found indeed a complete rupture of the uterus, but not at the site of the old scar, which was perfectly sound and undamaged. The rent was situated in another part of the uterus altogether. It was in the posterior wall of the uterus, and it was so large that the baby, weighing 8 lb., and the placenta had both passed through it into the general abdominal cavity. It was necessary to carry out hysterectomy, and the patient recovered. Incidentally, we used Australian Red Cross serum albumin for this operation from a supply most generously donated by the Australian Red Cross Society.

Comment.

I report the case because it demonstrates how soundly the lower segment Cæsarean incision can heal, when it is thus proved able to withstand the unfair test of an absolutely unsupervised obstructed labour, in which the contractions were so powerful that they tore the uterus open in another area. Undoubtedly the lower segment scar does disintegrate sometimes. I myself have seen this happen, but such an accident is very rare. The case I have reported serves to illustrate Victor Bonney's dictum that "There is probably no tissue in the body that heals so perfectly as the uterine muscle" ("Textbook of Gynæcology", 6th Edition, page 457). I have only a limited access to the literature here, but what textbooks and journals I have been able to consult record no similar case to this.

Case II.

This was a case of spontaneous rupture of the uterus in pregnancy. The patient was a multipara with a history of two normal labours, and she came to our hospital three weeks ago, complaining of lower abdominal pain and vomiting. She said that she was four months pregnant and that fœtal movements could be felt. These, in fact, were heard, and faintly also the fœtal heart sounds were audible. The uterus, felt bimanually, was enlarged to the size of an 18 weeks' pregnancy, the cervical os was closed and there was no blood on the examining finger. But the lower abdomen was tender, and this important sign I could not explain. Although the true diagnosis was not at this moment even suspected, the patient was asked to come into hospital for further observation. This she refused to do, saying that she had no money, and promising to return if the pain became worse. Her pulse rate was then 88 per minute and her blood pressure 110/80. Eight hours later she returned, but now in a state of profound collapse. A provisional diagnosis of rupture of the sac of a secondary abdominal pregnancy was made, and after the patient had been resuscitated, again with Australian Red Cross serum albumin, her abdomen was opened. The findings were a surprise. Obscured by five pints of fresh blood, which were floating freely in the abdomen, there was a 17 weeks' pregnancy, and the fœtus and placenta were still within the uterus. But the uterus was of the arcuate variety, and at the very summit of each of the two domes of the abnormally developed fundus a spontaneous uterine rupture had occurred. Two holes, each the size of a two-shilling piece, greeted the eye, and through each rupture bright red blood was steadily dripping. As we watched, placental tissue and blood-clot were also being slowly extruded from the holes in the fundi. This was, therefore, plainly a case of double spontaneous rupture in pregnancy at the two fundi of an arcuate uterus.

Comment.

Most obstetricians have seen an occasional case of rupture of the uterus in pregnancy where the uterus has suffered previous damage from classical Cæsarean section, from extensive curettage or, very rarely, from deep penetration by a hydatidiform mole; but I have not been able to find any record in the literature available to me here of a case where two quite separate ruptures of the uterine wall have occurred in pregnancy, and arising simply in association with a uterine maldevelopment. Fletcher Shaw[1] and Donald[2] of Manchester have each described cases of uterine rupture in pregnancy at the site of the fusion of the Müllerian ducts; but so far as I can ascertain, in neither of these cases did two separate ruptures of the fundus occur away from the seat of junction of these rudimentary ducts.

It was possible to conserve our patient's uterus, and she has survived. Because the fundus was necrotic for a distance of half an inch around both ruptures, we found it necessary to amputate the fundi by a wedge resection medial to the openings of the Fallopian tubes into the uterus. By employing the round ligaments and the loose peritoneum reflected from the isthmus (lower segment), we were able to cover all the raw areas of the repaired uterus with peritoneum.

[1] *J. Obstet. Gynæc. Brit. Emp.*, 1930, 37: 74.
[2] *Practitioner*, 1903, June.

I should be interested to know whether a double spontaneous rupture at the fundi of an arcuate uterus in pregnancy has been previously described. I am aware that McClintock, Master of the Rotunda Hospital, in his "Practical Observations on Midwifery", 1848, describes six cases of spontaneous rupture of the uterus in pregnancy, in Dublin, before the end of the fifth month, but he does not state whether the uterus was abnormally developed in any of these cases.

Yours, etc.,

R. H. J. HAMLIN.

The Princess Tsahai Hospital,
Addis Ababa,
Ethiopia.
December 20, 1960.

Naval, Military and Air Force.

APPOINTMENTS.

THE following appointments, changes, etc., are published in the *Commonwealth of Australia Gazette*, No. 84, of December 15, 1960.

AUSTRALIAN MILITARY FORCES.

Citizen Military Forces.

Eastern Command.

Royal Australian Army Medical Corps (Medical).—2/79012 Lieutenant-Colonel G. Clifton-Smith, E.D., relinquishes command 8th Field Ambulance 30th June, 1960, and is appointed to command 5th Field Ambulance, 1st July, 1960. 2/100752 Lieutenant-Colonel R. D. Rothfield relinquishes command 5th Field Ambulance, 30th June, 1960.

The following appointments, changes, etc., are published in the *Commonwealth of Australia Gazette*, No. 1, of January 5, 1961.

AUSTRALIAN MILITARY FORCES.

Australian Regular Army.

Royal Australian Army Medical Corps (Medical).

The Short Service Commission granted to 3/40147 Captain (Temporary Major) R. H. Meyer is extended until 11th January, 1964.

To be Captain, 14th October, 1960, with a Short Service Commission for a period of two years and three months.—3/12034 Ian Robert Walker.

Citizen Military Forces.

Northern Command.

Royal Australian Army Medical Corps (Medical).—2/67481 Captain (provisionally) J. E. Binnie is transferred from the Royal Australian Army Medical Corps (Medical), (Eastern Command), 1st July, 1960, with regimental seniority in accordance with Army seniority (5th March, 1959). 1/39235 Captain (provisionally) D. J. Cohen relinquishes the provisional rank of Captain, 10th October, 1960, and is transferred to the Reserve of Officers (Royal Australian Army Medical Corps (Medical)) (Northern Command) in the honorary rank of Captain, 11th October, 1960. The provisional appointments of the following officers are terminated:—Captains 1/39222 W. J. Crawford, 1st April, 1960, 1/61868 R. W. Hay, 16th August, 1960, and 1/46882 K. R. Townley, 16th September, 1960. *To be Captains (provisionally)*—1/39222 William John Crawford, 2nd April, 1960, 1/61868 Robert Webb Hay, 17th August, 1960 and 1/46882 Kenneth Russell Townley, 17th Septemer, 1960. *To be Major, 7th October, 1960*—1/13388 Captain (Temporary Lieutenant-Colonel) C. G. D. Clarke, and retains the temporary rank of Lieutenant-Colonel.. *To be Major, 7th October, 1960*—1/39155 Captain (Temporary Major) B. H. Gutteridge.

Eastern Command.

Royal Australian Army Medical Corps (Medical).—2/146556 Lieutenant-Colonel A. G. Finley is appointed from the Reserve of Officers, and is appointed Assistant Director of Medical Services, Headquarters 1st Division, and to be Colonel, 15th August, 1960. 2/12699 Colonel T. J. Ritchie, E.D., relinquishes the appointment of Assistant Director of Medical Services, Headquarters 2nd Division, 19th October, 1960, and is transferred to the Reserve of Officers (Eastern Command) 20th October, 1960. 2/67481 Captain (Provisionally) J. E. Binnie is transferred to Royal Australian Army Medical Corps (Medical) (Northern Command), 1st July, 1960.

Southern Command.

Royal Australian Army Medical Corps (Medical).—3/157155 Colonel R. S. Lawson relinquishes command 2nd General Hospital, 30th June, 1960, and is transferred to the Reserve of Officers (Southern Command), 1st July, 1960. The following officers are transferred to the Reserve of Officers) (Royal Australian Army Medical Corps (Medical)) (Southern Command), 1st July, 1960:—Lieutenant-Colonels 3/92021 W. Rosenthal and 3/157152. J. E. Clarke. *To be Major, 1st July, 1960*—3/101036 Captain H. D. Breidahl.

Central Command.

Royal Australian Army Medical Corps (Medical).—4/32018 Captain B. L. Cornish is appointed from the Reserve of Officers, 5th October, 1960. *To be Major, 6th October, 1960*—4/35428 Captain K. F. Milne.

Reserve Citizen Military Forces.

Royal Australian Army Medical Corps (Medical).

The following officers are placed on the Retired List (Eastern Command), and are granted military titles equivalent to the substantive or honorary rank shown, with permission to wear the prescribed uniform, 29th February, 1960:

Captain J. W. Quilter and Lieutenant (Honorary Captain) N. J. Solomon.

The following officer is placed upon the Retired List (Eastern Command), and is granted military titles equivalent to the substantive or honorary rank shown, with permission to wear the prescribed uniform, 30th April, 1960:

Major E. F. L. Laurie.

The following officers are placed upon the Retired List (Eastern Command), and are granted military titles equivalent to the substantive or honorary rank shown, with permission to wear the prescribed uniform, 30th June, 1960.

Lieutenant-Colonel H. I. Turnbull and Major C. A. McDermott.

ROYAL AUSTRALIAN AIR FORCE.

Permanent Air Force.

Medical Branch.

The following Squadron Leaders (acting Wing Commanders) are promoted to the rank of Wing Commander:—A. Cameron (039928), E. H. Stephenson (0312182).

The following Flight Lieutenants are promoted to the rank of Squadron Leader:—D. E. Charlton (0219360), K. N. Maunder (0217162), R. W. Plowright (0310776).

Post-Graduate Work.

AUSTRALIAN VICE-CHANCELLORS' COMMITTEE.

Nuffield Dominions Trust: Appointment at Oxford Medical School.

THE Registrar of the University of Oxford has advised that nominations are now invited from Australian universities to fill one appointment in the Oxford Medical School in the academic year beginning next October. The appointment is for one demonstratorship tenable in any one of the following departments: human anatomy; biochemistry (three-year tenure preferred); pharmacology; physiology. The appointment will be tenable for either two or three years, whichever is more convenient to the nominating university. Applicants are requested to indicate clearly the period of appointment agreeable to their university.

Medical deans have been supplied with information on the main research topics current in these departments. Duties will commence on October 1, 1961, or as soon thereafter as possible.

Conditions.

1. The qualifications for appointment to a demonstratorship shall be graduation at one of the Dominion universities and previous experience in research.

2. No person shall be appointed to a demonstratorship who does not intend that immediately after such appointment shall terminate he will return to the Dominion from which he was appointed for at least five years' work of a like nature as that carried out by him during his appointment.

Applications.

Letters of application, in duplicate, supported by the dean of the faculty of medicine in which the applicant trained or of the university with which the applicant is now associated, should be lodged with the Secretary, Australian Vice-Chancellors' Committee, c/o. University of Melbourne, Parkville, N.2, Victoria, not later than Friday, April 21, 1961.

Further information of the details and conditions of appointment under the Nuffield Dominions Trust may be obtained from the Registrar of each of the Australian universities.

WEEKLY SEMINARS AT THE INSTITUTE OF CLINICAL PATHOLOGY AND MEDICAL RESEARCH AND LIDCOMBE STATE HOSPITAL, SYDNEY.

THE following is the programme of seminars at the Institute of Clinical Pathology and Medical Research, Lidcombe, for the first term of 1961. These seminars are jointly sponsored by the Institute and by the State Hospital, Lidcombe, and are held each Monday at 3.30 p.m. in the Institute's Lecture Room:

February 6: "Connective Tissue", Dr. H. Kramer, Institute of Clinical Pathology and Medical Research.

February 13: "Synthesis and Abnormalities of Human Hæmoglobin", Dr. W. Hensley, Department of Biochemistry, University of Sydney.

February 20: "Ulceration of the Lower Limb", Dr. I. J. Hunter, Institute of Clinical Pathology and Medical Research, and Dr. R. Holland, The State Hospital, Lidcombe.

February 27: "Œdema, Diuresis and Diuretics", Dr. N. F. R. Fink, The State Hospital, Lidcombe.

March 6: "Human Chromosomes", Dr. Brian Turner, Neuropathologist, Psychiatric Centre, North Ryde, and Dr. G. C. Hughes, The State Hospital, Lidcombe.

March 13: Symposium on poliomyelitis: "Public Health and Epidemiological Aspects", Dr. E. S. A. Meyers, Department of Public Health; "The Polio Viruses", Mr. A. M. Murphy, Institute of Clinical Pathology and Medical Research; "Pathology", Dr. I. J. Hunter, Institute of Clinical Pathology and Medical Research.

March 20: "Urinary Retention in the Elderly Male", Dr. T. L. O'Connell, The State Hospital, Lidcombe.

March 27: "The Quest for Rejuvenation", Dr. R. Holland and Dr. F. Ofner, The State Hospital, Lidcombe.

April 10: "The Role of the Aged in Society", Dr. C. J. Cummins, Director General of Public Health.

April 17: "Skin Cancers II", Dr. V. St. E. D'Abrera, Institute of Clinical Pathology and Medical Research.

April 24: Symposium on emphysema: "Pathology", Dr. P. Harden, Institute of Clinical Pathology and Medical Research; "Physiology", Dr. B. E. Sharkey, The State Hospital, Lidcombe; "Management", Dr. G. E. Kellerman, The State Hospital, Lidcombe.

May 1: "Physical Signs in Clinical Medicine", Dr. G. S. Procopis, The State Hospital, Lidcombe.

POST-GRADUATE F.O.C.L.A. COURSE.

The tenth annual Post-Graduate F.O.C.L.A. Course, organized by the Federation of Country Local Associations in New South Wales, will be held at Goulburn, N.S.W., from March 20 to 24, 1961. The general title of the course will be "Accidents and Trauma".

The course will be opened at 10 a.m. on Monday, March 20, by the State Minister for Health, Mr. W. F. Sheahan. This will be followed at 11.30 a.m. by the Mulvey Oration, delivered by Dr. J. H. Coles. Lecturers will include Dr. W. A. Conolly, Dr. B. E. Dwyer, Dr. John Greenaway, Dr. P. Heery, Dr. Douglas Miller, Dr. S. E. J. Robertson and Dr. A. Rumore. One afternoon will be given over to a lecture and demonstration at Kenmore Hospital by Dr. D. R. Morgan and members of the staff.

The course secretary is Dr. B. W. Coombes, McKell Place, Goulburn.

Public Health.

POLICE OFFENCES (AMENDMENT) ACT, 1908, AS AMENDED, OF NEW SOUTH WALES.

THE Under Secretary, Chief Secretary's Department of New South Wales, has requested that publicity be given to the following proclamation, gazetted on Friday, December 23, 1960, applying Part VI of the *Police Offences (Amendment) Act* to diphenoxylate. The proclamation is to take effect from July 3, 1961.

PROCLAMATION.

(L.S.)
E. W. WOODWARD.
GOVERNOR.

I, Lieutenant-General Sir Eric Winslow Woodward, Governor of the State of New South Wales, with the advice of the Executive Council do, by this my Proclamation, declare that Part VI of this Police Offences (Amendment) Act, 1908 as amended, shall apply to:—

DIPHENOXYLATE (1-(3, 3-diphenyl-3-cyanoprophyl)-4-phenylpiperidine-4-carboxylic acid ethyl ester, its salts and any preparation, admixture, extract or other substance containing Diphenoxylate,

in the same manner as it applies to the drugs mentioned in paragraph (a) of subsection (2) of Section 18 of the said Act.

I hereby declare that this my Proclamation shall take effect on and from Monday, 3rd July, 1961.

Signed and sealed this seventh day of December, One thousand nine hundred and sixty.

By His Excellency's Command,
C. A. KELLY.

GOD SAVE THE QUEEN!

Australian Medical Board Proceedings.

NEW SOUTH WALES.

THE following additions and amendments have been made to the Register of Medical Practitioners for New South Wales, in accordance with the provisions of the *Medical Practitioners Act*, 1938-1958.

Registered medical practitioners who have complied with the requirements of Section 17 (3) and are registered under Section 17 (1) (*a*) of the Act: Balmer, Vivian George, M.B., B.S., 1951 (Univ. Melbourne), D.A., R.C.P. & S. (England), 1958, F.F.A., R.A.C.S., 1960; Bricknell, Judith Ann, M.B., B.S., 1956 (Univ. Queensland), Irvine-Brown, Malcolm, M.B., B.S., 1955 (Univ. Queensland), Mann, Arnold, M.B., B.S., 1953 (Univ. Melbourne).

Registered medical practitioners who have complied with the requirements of Section 17 (3) and are registered under Section 17 (1) (*b*) of the Act: Cumming, Christian Ruth, L.M.S.S.A., 1948, M.R.C.S. (England), L.R.C.P. (London), 1948; Douglas, Alexander, M.B., Ch.B., 1946 (Univ. St. Andrews), D.P.H. (St. Andrews), 1949, D.T.M. & H., R.C.P. & S. (England), 1950; Duncan, Margaret, M.B., Ch.B., 1951 (Univ. Edinburgh), D.P.H. (London), 1958; Jones, Arnold, M.B., Ch.B., 1957 (Univ. Birmingham); Killick, John Francis, M.B., Ch.B., 1950 (Univ. Edinburgh); McCarthy, Nora Millicent, M.B., B.Ch., 1955 (N. Univ. Ireland), D.A., R.C.P. & S. (England), 1959; McFarlane, Robin Sproul, M.R.C.S. (England), L.R.C.P. (London), 1959, M.B., B.S., 1959 (Univ. London); Packham, Arthur Lewis Christopher, M.B., B.S., 1950 (Univ. London); Quantrill, John Richard Yarr, M.B., B.Ch., 1951 (Univ. Witwatersrand), D.P.H. (Witwatersrand), 1955; Taylor, John Morcom, M.B., Ch.B., 1958 (Univ. Liverpool), M.R.C.S. (England), L.R.C.P. (London), 1958; Watkins, Wolfe Kildare Milton Colston, M.B., Ch.B., 1948 (Univ. Liverpool), M.R.C.S. (England), L.R.C.P. (London), 1948, F.R.C.S. (England), 1957, F.R.C.S. (Edinburgh), 1957.

Registered medical practitioners who have complied with the requirements of Section 17 (3) and are registered under Section 17 (1) (*f*) of the Act: Klavins, Arvids, M.D., 1928 (Univ. Riga); Rec, Otakar, M.D., 1948 (Univ. Heidelberg); Stepan, Jaromira Frances, M.D., 1946 (Univ. Prague); Wouters, Labora Marianne, M.D., 1949 (Univ. Vienna).

Registered medical practitioners who have complied with the requirements of Section 17 (3) and are registered under Section 17 (2A) of the Act: Babajews, Alexander, M.D., 1937 (Univ. Baku); Selecki, Borys Romuald, M.D., 1951 (Univ. Wroclaw).

The following have been issued with a licence under Section 21A of the Act: Csillag, John, one year from December 1, 1960; Frommer, John Eugene, one year from December 1, 1960.

The following have been issued with a licence under Section 21C (4) of the Act: Banathy, Laszlo Julius Joseph, for a period from November 7, 1960, to October 6, 1961; Luedecki, Hans, for a period of one year from September 1, 1960; Peukert, Joseph, for a period from November 1, 1960 to October 20, 1961; Nagy, Laszlo, for a period from November 14, 1960 to April 22, 1961; Alexander, M. S., for a period from November 21, 1960 to August 17, 1961.

The following have been issued with a licence under Section 21C (3) of the Act: Bordeinei, Oleg, for a period of one year from November 14, 1960; Foscolos, Paul, for a period of one year from November 21, 1960.

The following has been issued with an Interim Licence under Section 21C (3) of the Act: Jandy, Zygmunt, St. Joseph's Hospital, Auburn.

Notes and News.

Australian of the Year, 1960.

Sir Macfarlane Burnet, Director of the Walter and Eliza Hall Institute of Medical Research, has been declared Australian of the Year for 1960 by the Australia Day Council.

The Metric System at the Royal Adelaide Hospital.

According to an announcement in the Adelaide *Advertiser* on January 5, 1961, the Royal Adelaide Hospital will adopt the metric system of weights and measures from July 1. The Queen Elizabeth Hospital in the same city has been using the metric system since it opened a few years ago.

Monash University: Chair of Anatomy.

Dr. G. C. Schofield has been appointed to the chair of anatomy at Monash University, Melbourne. He is a graduate of the University of Otago Medical School.

University of New Zealand: Diploma in Obstetrics.

A course in obstetrics for the diploma in obstetrics of the University of New Zealand will be held at the Post-Graduate School of Obstetrics and Gynæcology of the University of Auckland, National Women's Hospital, Green Lane West, Auckland, from February 25 to March 3, 1961. The course is of interest to general practitioners. The written examination will be held in both Auckland and Dunedin on March 6. The clinical and oral examinations will be conducted in Auckland on March 7 and 8. Further information may be obtained from the Registrar, University of Auckland.

Sir David Wilkie Research Fellowship.

The Faculty of Medicine of the University of Edinburgh announces that the Sir David Wilkie Research Fellowship in surgery and/or medicine, of the value of £800 to £900 (sterling) *per annum*, with a possible allowance for approved expenses of research, and tenable for two years (with possible extension to three years at the discretion of the Senatus Academicus), will be open for award in October, 1961. The fellowship is open to graduates of any university who wish to obtain training in research in surgery and/or medicine. The holder will be required to carry out approved research work in surgery and/or medicine in the University, and he must attend the honours class in physiology, unless he is already a graduate in physiology or in science. While undertaking the research work he will be expected to maintain contact with clinical work, but the time to be devoted to this will be restricted to two half-days per week. During his tenure the Fellow will not be permitted to

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED DECEMBER 24, 1960.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.[2]	Northern Territory.	Australian Capital Territory.	Australia.[2]
Acute Rheumatism	1	..	2(2)	..	..	..	1	..	4
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	..	..	1(1)	..	..	..	4	..	5
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	1	2(1)	..	..	..	..	..	..	3
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	4(3)	1(1)	..	..	..	..	3	5	13
Diphtheria	..	1(1)	..	..	1(1)	..	..	..	2
Dysentery (Bacillary)	..	..	..	1(1)	7(1)	..	1	1	10
Encephalitis	1	..	..	..	..	..	..	..	1
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	1	..	..	..	..	..	..	1
Infective Hepatitis	173(97)	54(24)	23(7)	47(13)	15(5)	..	1	8	316
Lead Poisoning	..	..	1	..	..	..	..	..	1
Leprosy	..	..	..	..	2	..	1	..	3
Leptospirosis	..	..	1(1)	..	..	..	..	..	1
Malaria	..	..	..	..	..	..	..	..	..
Meningococcal Infection	..	..	..	..	..	..	..	..	..
Ophthalmia	..	..	..	..	..	..	..	7	7
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	..	1	..	..	1	..	..	..	2
Puerperal Fever	2	..	1	..	..	..	..	..	3
Rubella	..	13(5)	1(1)	..	7(7)	..	..	..	21
Salmonella Infection	..	..	..	2(2)	..	..	..	..	2
Scarlet Fever	10(6)	12(4)	3(1)	2(2)	..	..	..	..	27
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	1	3(2)	..	..	..	..	4
Trachoma	..	..	..	..	1	..	..	..	1
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	25(19)	10(8)	24(8)	6(3)	4(4)	..	..	2	71
Typhoid Fever	..	..	..	..	..	..	..	..	..
Typhus (Flea-, Mite- and Tick-borne)	..	..	..	..	..	..	..	..	..
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

[2] Figures incomplete owing to absence of return from Tasmania.

study for or to present himself for any examination leading to a higher diploma in medicine or surgery.

Applications must be submitted on a prescribed form, a copy of which may be obtained from the Dean of the Faculty of Medicine of the University of Edinburgh, or from the Chairman of the National Health and Medical Research Council, Department of Health, Canberra, A.C.T. Applications from graduates in Australia should reach the Chairman of the National Health and Medical Research Council by March 1, 1961.

Corrigenda.

PNEUMATOSIS CYSTOIDES INTESTINALIS (HOMINIS).

IN the article by A. Rumore entitled "Pneumatosis Cystoides Intestinalis (Hominis)" in the issue of January 7, 1961, Figure IV on page 16 was inadvertently printed upside down. We regret this error.

MICROCORNEAL CONTACT LENSES.

IN the article entitled "Microcorneal Contact Lenses", by Peter F. Anderson, in the issue of December 10, 1960, an error appears in line 5 of the paragraph headed "Aphakia and Anisometropia" on page 939. The sentence "the image of the aphakic eye is approximately three times larger than the image of the normal eye" should read "the image of the aphakic eye is aproximately one-third larger than the image of the normal eye".

MASSIVE CHEMOTHERAPY IN MALIGNANT DISEASE IN CHILDHOOD.

DR. DOUGLAS COHEN has advised us of an error in his paper on "Massive Chemotherapy in Malignant Disease in Childhood" in the issue of November 19, 1960. On page 808, in line 19 of the first column the dosage of T.E.M. is shown as 15 to 18 mg. per kilogram. This should be 1·5 to 1·8 mg. per kilogram.

Nominations and Elections.

THE following have applied for election as members of the New South Wales Branch of the British Medical Association:

Porter, Ronald Ernest, M.B., B.S., 1937 (Univ. Sydney), D.P.M., 1947 (Univ. Sydney), Bridge Road, Westmead.

Ma, King Yuk, M.B., B.S., 1959 (Univ. Sydney), Royal Newcastle Hospital, Newcastle.

Chung, Robert Milton, M.B., B.S., 1960 (Univ. Sydney), Lewisham Hospital, Lewisham.

Godfrey, Howard Fuller, M.B., B.S., 1959 (Univ. Sydney), Women's Hospital, Crown Street, Sydney.

Gordon, Robert Gabriel, M.B., B.S., 1960 (Univ. Sydney), 3/31 Roscoe Street, Bondi.

The undermentioned have been elected members of the New South Wales Branch of the British Medical Association:

Banathy, Laszlo Julius Joseph, M.D., 1944 (Univ. Debrecen), Reg. Licence Section 21 c (4), *Medical Practitioners Act*, 1938-1958; Chapman, Francis Clement, M.B., B.S., 1957 (Univ. Sydney); Fleming, Janet Allene, M.B., B.S., 1959; Fraser, Robin, M.B., B.S., 1958 (Univ. Sydney); Halmagyi, Alice Julia, M.D., 1947 (Univ. Szeged), Reg. 17 2A, *Medical Practitioners Act*; Holland, John Terence, M.B., B.S., 1955 (Univ. Sydney), B.Sc. (Med.), 1953; Kalokerinos, Archivides, M.B., B.S., 1951 (Univ. Sydney); Landecker, Kathrine Dorothy, M.B., B.S., 1959 (Univ. Sydney); McGuire, Peter Neville, M.B., B.S., 1959 (Univ. Sydney); Nicholl, Neil Livingstone, M.B., B.S., 1958 (Univ. Queensland); Ramsay, Helen McGregor, M.B., B.S., 1952 (Univ. Sydney); Roberts, Harley Stuart, M.B., B.S., 1959 (Univ Sydney); Rush, Bryan McKay, M.B., B.S., 1957 (Univ. Sydney); Taylor, Roger Bruce, M.B., B.S., 1959 (Univ. Sydney).

Deaths.

THE following death has been announced:

SHAW.—Robert de Courcy Shaw, on January 13, 1961, at Melbourne.

Diary for the Month.

FEBRUARY 1.—Western Australian Branch, B.M.A.: Branch Council Meeting.
FEBRUARY 2.—South Australian Branch, B.M.A.: Council Meeting.
FEBRUARY 7.—New South Wales Branch, B.M.A.: Organization and Science Committee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

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ALL articles submitted for publication in this Journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations, other than those normally used by the Journal, and not to underline either words or phrases.

Authors of papers are asked to state for inclusion in the title their principal qualifications as well as their relevant appointment and/or the unit, hospital or department from which the paper comes.

References to articles and books should be carefully checked. In a reference to an article in a journal the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of article. In a reference to a book the following information should be given: surname of author, initials of author, year of publication, full title of book, publisher, place of publication, page number (where relevant). The abbreviations used for the titles of journals are those of the list known as "World Medical Periodicals" (published by the World Medical Association). If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full data in each instance.

Authors submitting illustrations are asked, if possible, to provide the originals (not photographic copies) of line drawings, graphs and diagrams, and prints from the original negatives of photomicrographs. Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary is stated.

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